

chain nodes :

6 7 8 27 28 29 30 35

ring nodes :

1 2 3 4 5 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26

chain bonds :

1-6 4-35 6-7 6-8 9-27 15-28 21-29 29-30

ring bonds :

1-2 1-5 2-3 3-4 4-5 9-10 9-14 10-11 11-12 12-13 13-14 15-16 15-20 16-17
17-18 18-19 19-20 21-22 21-26 22-23 23-24 24-25 25-26

exact/norm bonds :

1-2 2-3 4-35 6-7 6-8 9-27 15-16 15-20 15-28 16-17 17-18 18-19 19-20 21-29
29-30

exact bonds :

1-5 1-6 3-4 4-5

normalized bonds :

9-10 9-14 10-11 11-12 12-13 13-14 21-22 21-26 22-23 23-24 24-25 25-26

isolated ring systems :

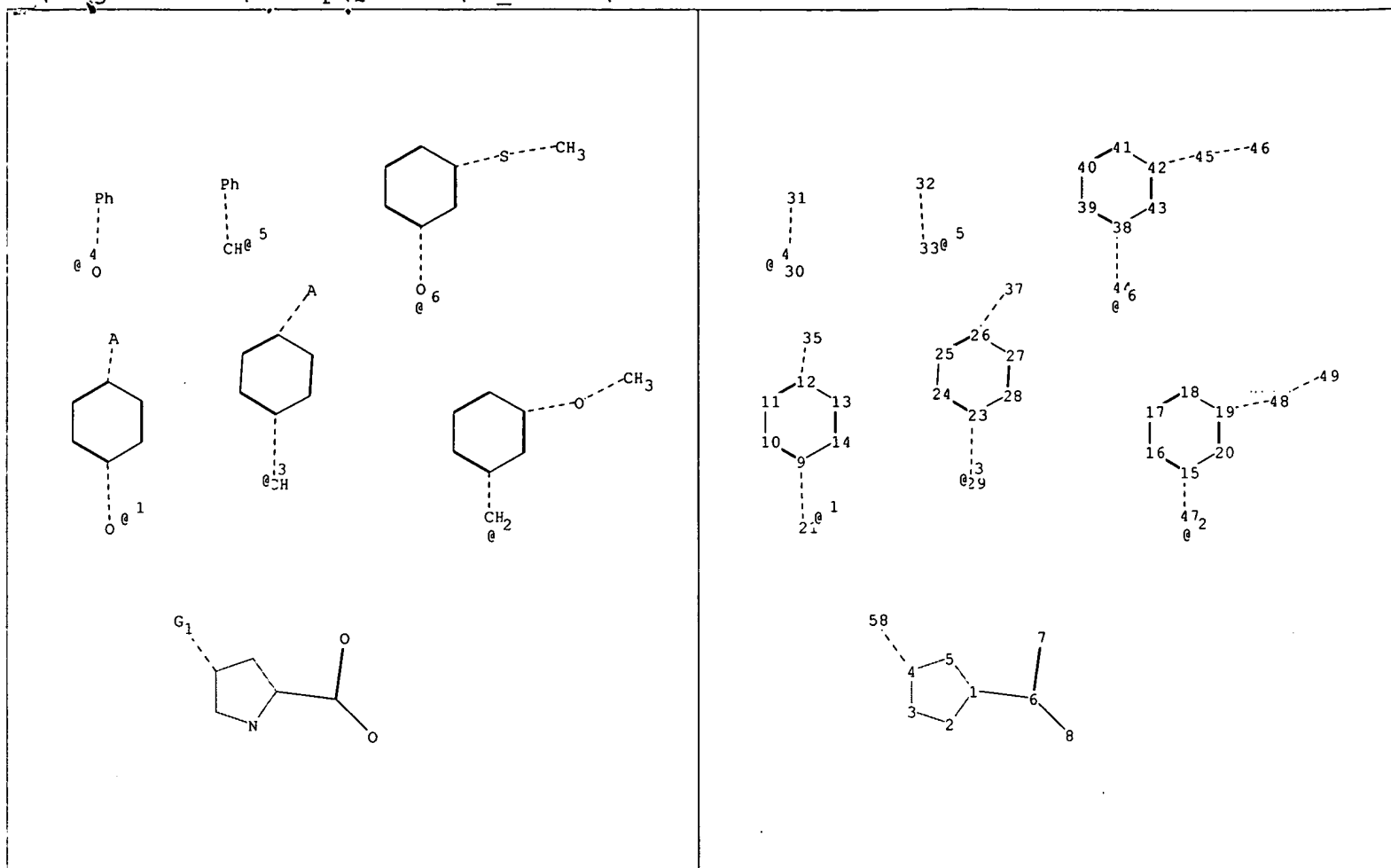
containing 1 :

G1: [*1], [*2], [*3]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom
21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:CLASS 28:CLASS 29:CLASS
30:CLASS 35:CLASS

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chain nodes :

6 7 8 21 29 30 31 32 33 44 45 46 47 48 49 58

ring nodes :

1 2 3 4 5 9 10 11 12 13 14 15 16 17 18 19 20 23 24 25 26 27 28 38
39 40 41 42 43

ring/chain nodes :

35 37

chain bonds :

1-6 4-58 6-7 6-8 9-21 12-35 15-47 19-48 23-29 26-37 30-31 32-33 38-44 42-45
45-46 48-49

ring bonds :

1-2 1-5 2-3 3-4 4-5 9-10 9-14 10-11 11-12 12-13 13-14 15-16 15-20 16-17
17-18 18-19 19-20 23-24 23-28 24-25 25-26 26-27 27-28 38-39 38-43 39-40 40-41
41-42 42-43

exact/norm bonds :

1-2 2-3 4-58 6-7 6-8 9-21 12-35 15-47 19-48 23-29 26-37 30-31 32-33 38-44
42-45 45-46 48-49

exact bonds :

1-5 1-6 3-4 4-5

normalized bonds :

9-10 9-14 10-11 11-12 12-13 13-14 15-16 15-20 16-17 17-18 18-19 19-20 23-24
23-28 24-25 25-26 26-27 27-28 38-39 38-43 39-40 40-41 41-42 42-43

isolated ring systems :

containing 1 :

G1: [*1], [*2], [*3], [*4], [*5], [*6]

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Connectivity :

10:2 E exact RC ring/chain 11:2 E exact RC ring/chain 13:2 E exact RC ring/chain
14:2 E exact RC ring/chain 16:2 E exact RC ring/chain 17:2 E exact RC ring/chain
18:2 E exact RC ring/chain 20:2 E exact RC ring/chain 24:2 E exact RC ring/chain
25:2 E exact RC ring/chain 27:2 E exact RC ring/chain 28:2 E exact RC ring/chain
39:2 E exact RC ring/chain 40:2 E exact RC ring/chain 41:2 E exact RC ring/chain
43:2 E exact RC ring/chain

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom
21:CLASS 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:CLASS 30:CLASS
31:CLASS 32:CLASS 33:CLASS 35:CLASS 37:CLASS 38:Atom 39:Atom 40:Atom 41:Atom
42:Atom 43:Atom 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS 49:CLASS 58:CLASS

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Search history

Jones 10/698354

03/10/2006

=> d his full

(FILE 'HOME' ENTERED AT 09:30:38 ON 10 MAR 2006)

L1 FILE 'REGISTRY' ENTERED AT 09:31:20 ON 10 MAR 2006
L2 STRUCTURE UPLOADED
50 SEA SSS SAM L1

FILE 'STNGUIDE' ENTERED AT 09:35:43 ON 10 MAR 2006

L3 FILE 'CAPLUS' ENTERED AT 09:36:17 ON 10 MAR 2006
33 SEA ABB=ON PLU=ON L2
D STAT QUE L2

FILE 'STNGUIDE' ENTERED AT 09:36:50 ON 10 MAR 2006
D SCA L2

FILE 'REGISTRY' ENTERED AT 09:38:58 ON 10 MAR 2006

FILE 'STNGUIDE' ENTERED AT 09:38:59 ON 10 MAR 2006
D SCA L2

FILE 'REGISTRY' ENTERED AT 09:39:05 ON 10 MAR 2006

FILE 'STNGUIDE' ENTERED AT 09:41:56 ON 10 MAR 2006
D SCA L2

L4 FILE 'REGISTRY' ENTERED AT 09:42:03 ON 10 MAR 2006
1152 SEA SSS FUL L1
SAVE TEMP L4 JON354STRA/A

L5 FILE 'CAPLUS' ENTERED AT 09:45:31 ON 10 MAR 2006
219 SEA ABB=ON PLU=ON L4

FILE 'REGISTRY' ENTERED AT 09:45:44 ON 10 MAR 2006

FILE 'CAPLUS' ENTERED AT 09:46:17 ON 10 MAR 2006

FILE 'STNGUIDE' ENTERED AT 09:46:58 ON 10 MAR 2006

L6 FILE 'CAPLUS' ENTERED AT 09:47:33 ON 10 MAR 2006
E US2003-698354/APPS
1 SEA ABB=ON PLU=ON US2003-698354/AP
D SCA
SEL RN

L7 FILE 'REGISTRY' ENTERED AT 09:48:09 ON 10 MAR 2006
95 SEA ABB=ON PLU=ON (100-39-0/BI OR 100-53-8/BI OR 102195-80-2/
BI OR 105107-84-4/BI OR 106-48-9/BI OR 106-53-6/BI OR 108-42-9/
BI OR 108-43-0/BI OR 159418-27-6/BI OR 159418-50-5/BI OR
163190-46-3/BI OR 163190-47-4/BI OR 170850-75-6/BI OR 2216-51-5
/BI OR 227935-38-8/BI OR 23681-89-2/BI OR 262843-21-0/BI OR
344286-69-7/BI OR 356558-26-4/BI OR 367-12-4/BI OR 372-20-3/BI
OR 487048-23-7/BI OR 54631-82-2/BI OR 58632-55-6/BI OR
622-95-7/BI OR 686766-25-6/BI OR 686766-26-7/BI OR 686766-27-8/
BI OR 686766-28-9/BI OR 686766-29-0/BI OR 686766-30-3/BI OR
686766-31-4/BI OR 686766-32-5/BI OR 686766-33-6/BI OR 686766-34
-7/BI OR 686766-35-8/BI OR 686766-36-9/BI OR 686766-37-0/BI OR
686766-38-1/BI OR 686766-39-2/BI OR 686766-40-5/BI OR 686766-41
-6/BI OR 686766-42-7/BI OR 686766-43-8/BI OR 686766-44-9/BI OR

g-h

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686766-45-0/BI OR 686766-46-1/BI OR 686766-47-2/BI OR 686766-48-3/BI OR 686766-49-4/BI OR 686766-50-7/BI OR 686766-51-8/BI OR 686766-52-9/BI OR 686766-53-0/BI OR 686766-54-1/BI OR 686766-55-2/BI OR 686766-56-3/BI OR 686766-57-4/BI OR 686766-58-5/BI OR 686766-59-6/BI OR 686766-60-9/BI OR 686766-61-0/BI OR 686766-62-1/BI OR 686766-63-2/BI OR 686766-64-3/BI OR 686766-65-4/BI OR 686766-66-5/BI OR 686766-67-6/BI OR 686766-68-7/BI OR 686766-69-8/BI OR 686766-70-1/BI OR 686766-71-2/BI OR 686766-72-3/BI OR 686766-73-4/BI OR 686766-74-5/BI OR 686766-75-6/BI OR 686766-76-7/BI OR 686766-77-8/BI OR 686766-78-9/BI OR 686766-79-0/BI OR 686766-80-3/BI OR 686766-81-4/BI OR 686766-82-5/BI OR 686766-84-7/BI OR 686766-86-9/BI OR 686766-87-0/BI OR 688007-58-1/BI OR 688007-59-2/BI OR 688007-60-5/BI OR 72311-12-7/BI OR 74844-91-0/BI OR 83623-88-5/BI OR 83624-62-8/BI OR 88043-21-4/BI OR 89302-81-8/BI)

L8 52 SEA ABB=ON PLU=ON L7 AND L4

FILE 'CAPLUS' ENTERED AT 09:49:14 ON 10 MAR 2006
D SCA L6

L9 55 SEA ABB=ON PLU=ON L4 (L) THU/RL

L10 462 SEA ABB=ON PLU=ON L7 (L) THU/RL

L11 8 SEA ABB=ON PLU=ON L9 AND L10
D SCA

FILE 'STNGUIDE' ENTERED AT 09:54:56 ON 10 MAR 2006

FILE 'REGISTRY' ENTERED AT 10:10:23 ON 10 MAR 2006

FILE 'STNGUIDE' ENTERED AT 10:10:25 ON 10 MAR 2006

FILE 'CAPLUS' ENTERED AT 10:21:46 ON 10 MAR 2006
L12 13 SEA ABB=ON PLU=ON L8

FILE 'REGISTRY' ENTERED AT 10:25:48 ON 10 MAR 2006
D SCA L8

L13 393 SEA ABB=ON PLU=ON L4 AND A7/PG

FILE 'CAPLUS' ENTERED AT 10:42:02 ON 10 MAR 2006
L14 98 SEA ABB=ON PLU=ON L13

FILE 'STNGUIDE' ENTERED AT 10:45:47 ON 10 MAR 2006

FILE 'REGISTRY' ENTERED AT 11:04:56 ON 10 MAR 2006
L*** DEL STRUCTURE UPLOADED
L15 STRUCTURE UPLOADED
L16 38 SEA SUB=L4 SSS SAM L15
L17 751 SEA SUB=L4 SSS FUL L15
L18 401 SEA ABB=ON PLU=ON L4 NOT L17

FILE 'CAPLUS' ENTERED AT 11:08:15 ON 10 MAR 2006
L19 104 SEA ABB=ON PLU=ON L18

FILE 'REGISTRY' ENTERED AT 11:08:31 ON 10 MAR 2006

FILE 'CAPLUS' ENTERED AT 11:11:41 ON 10 MAR 2006
SEL RN L19
DELETE SELECT

FILE 'REGISTRY' ENTERED AT 11:12:57 ON 10 MAR 2006
SAVE TEMP L17 JON354STRC/A

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L20 STRUCTURE UPLOADED
 L21 42 SEA SUB=L4 SSS SAM L20
 L22 820 SEA SUB=L4 SSS FUL L20
 SAVE TEMP JON354STRD/A L22
 L23 332 SEA ABB=ON PLU=ON L4 NOT L22

FILE 'CAPLUS' ENTERED AT 11:20:18 ON 10 MAR 2006

L24 71 SEA ABB=ON PLU=ON L23
 L25 13 SEA ABB=ON PLU=ON L12 AND L24
 L26 58 SEA ABB=ON PLU=ON L24 NOT L25
 D COST

FILE 'STNGUIDE' ENTERED AT 11:23:48 ON 10 MAR 2006

FILE 'REGISTRY' ENTERED AT 11:25:03 ON 10 MAR 2006

FILE 'CAPLUS' ENTERED AT 11:28:08 ON 10 MAR 2006

L27 101 SEA ABB=ON PLU=ON RAWSON D?/AU
 L28 1 SEA ABB=ON PLU=ON L27 AND L12
 L29 1 SEA ABB=ON PLU=ON L27 AND L24
 D SCA L6
 L*** DEL 0 S PROLINE/CT
 L30 38144 SEA ABB=ON PLU=ON PROLINE/OBI
 L31 1 SEA ABB=ON PLU=ON L27 AND L30
 L32 754958 SEA ABB=ON PLU=ON CALCIUM/BI
 L33 4 SEA ABB=ON PLU=ON L27 AND L32
 L34 65985 SEA ABB=ON PLU=ON PROLINE/BI
 L35 1 SEA ABB=ON PLU=ON L27 AND L34
 L36 86979 SEA ABB=ON PLU=ON 34/CC
 L37 3 SEA ABB=ON PLU=ON L36 AND L27
 L38 990634 SEA ABB=ON PLU=ON 1/CC
 L39 348762 SEA ABB=ON PLU=ON 63/CC
 L40 3 SEA ABB=ON PLU=ON L27 AND (L38 OR L39)

FILE 'REGISTRY' ENTERED AT 11:36:39 ON 10 MAR 2006

L41 44 SEA ABB=ON PLU=ON L8 NOT L22

FILE 'CAPLUS' ENTERED AT 11:37:58 ON 10 MAR 2006

L42 10 SEA ABB=ON PLU=ON L41
 L43 10 SEA ABB=ON PLU=ON L42 AND L24
 L44 1 SEA ABB=ON PLU=ON L27 AND L42

FILE 'STNGUIDE' ENTERED AT 11:41:06 ON 10 MAR 2006

FILE 'REGISTRY' ENTERED AT 11:42:35 ON 10 MAR 2006

D STAT QUE L4
 D STAT QUE L23

FILE 'STNGUIDE' ENTERED AT 11:43:00 ON 10 MAR 2006

FILE 'CAPLUS' ENTERED AT 11:44:56 ON 10 MAR 2006

D QUE NOS L31
 D QUE NOS L33
 D QUE NOS L29
 D QUE NOS L35
 D QUE NOS L37
 D QUE NOS L40
 D QUE NOS L44

L45 9 SEA ABB=ON PLU=ON L44 OR L29 OR L31 OR L33 OR L35 OR L37 OR
 L40

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D IBIB ABS HITIND HITSTR L45 1-9

FILE 'STNGUIDE' ENTERED AT 11:46:15 ON 10 MAR 2006

FILE 'CAPLUS' ENTERED AT 11:47:11 ON 10 MAR 2006

D QUE NOS L42

D QUE NOS L43

L46 9 SEA ABB=ON PLU=ON ((L42 OR L43)) NOT L45
 D IBIB ABS HITIND HITSTR L46 1-9

FILE 'STNGUIDE' ENTERED AT 11:48:25 ON 10 MAR 2006

FILE 'CAPLUS' ENTERED AT 11:49:05 ON 10 MAR 2006

D QUE NOS L24

L47 61 SEA ABB=ON PLU=ON L24 NOT (L45 OR L46)
 D IBIB ABS HITIND HITSTR L47 1-61

FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 8 MAR 2006 HIGHEST RN 876273-86-8

DICTIONARY FILE UPDATES: 8 MAR 2006 HIGHEST RN 876273-86-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

*

* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

FILE STNGUIDE

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Mar 3, 2006 (20060303/UP).

FILE CAPLUS

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FILE COVERS 1907 - 10 Mar 2006 VOL 144 ISS 12
FILE LAST UPDATED: 9 Mar 2006 (20060309/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=>

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=> file registry
FILE 'REGISTRY' ENTERED AT 11:42:35 ON 10 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE QUERIES

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 8 MAR 2006 HIGHEST RN 876273-86-8
DICTIONARY FILE UPDATES: 8 MAR 2006 HIGHEST RN 876273-86-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

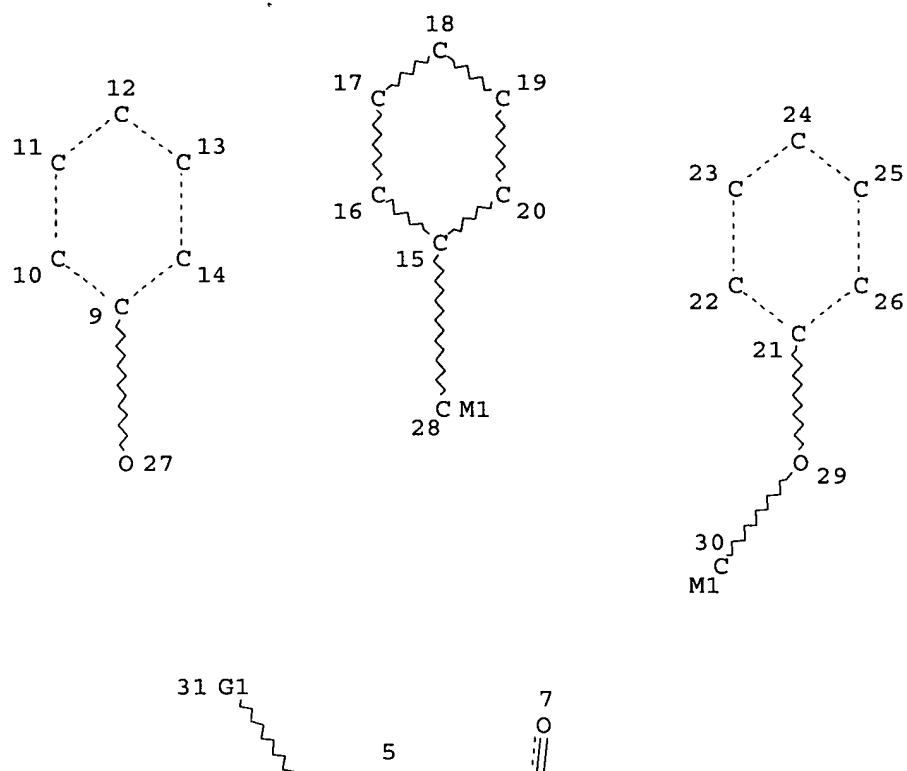
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS
for details.

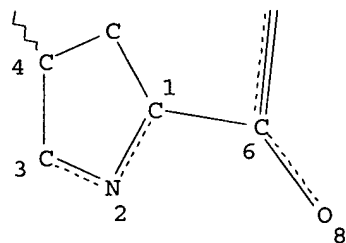
REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> d stat que L4
L1 STR



Page 1-A



Page 2-A

VAR G1=27/28/30

NODE ATTRIBUTES:

HCOUNT	IS	M1	AT	28
HCOUNT	IS	M1	AT	30
NSPEC	IS	R	AT	1
NSPEC	IS	R	AT	2
NSPEC	IS	R	AT	3
NSPEC	IS	R	AT	4
NSPEC	IS	R	AT	5
NSPEC	IS	C	AT	6
NSPEC	IS	C	AT	7
NSPEC	IS	C	AT	8
NSPEC	IS	R	AT	9
NSPEC	IS	R	AT	10
NSPEC	IS	R	AT	11
NSPEC	IS	R	AT	12
NSPEC	IS	R	AT	13

NSPEC IS R AT 14
NSPEC IS R AT 15
NSPEC IS R AT 16
NSPEC IS R AT 17
NSPEC IS R AT 18
NSPEC IS R AT 19
NSPEC IS R AT 20
NSPEC IS R AT 21
NSPEC IS R AT 22
NSPEC IS R AT 23
NSPEC IS R AT 24
NSPEC IS R AT 25
NSPEC IS R AT 26
NSPEC IS C AT 27
NSPEC IS C AT 28
NSPEC IS C AT 29
NSPEC IS C AT 30
NSPEC IS C AT 31
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 6 7 8 27 28 29 30
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 1
NUMBER OF NODES IS 31

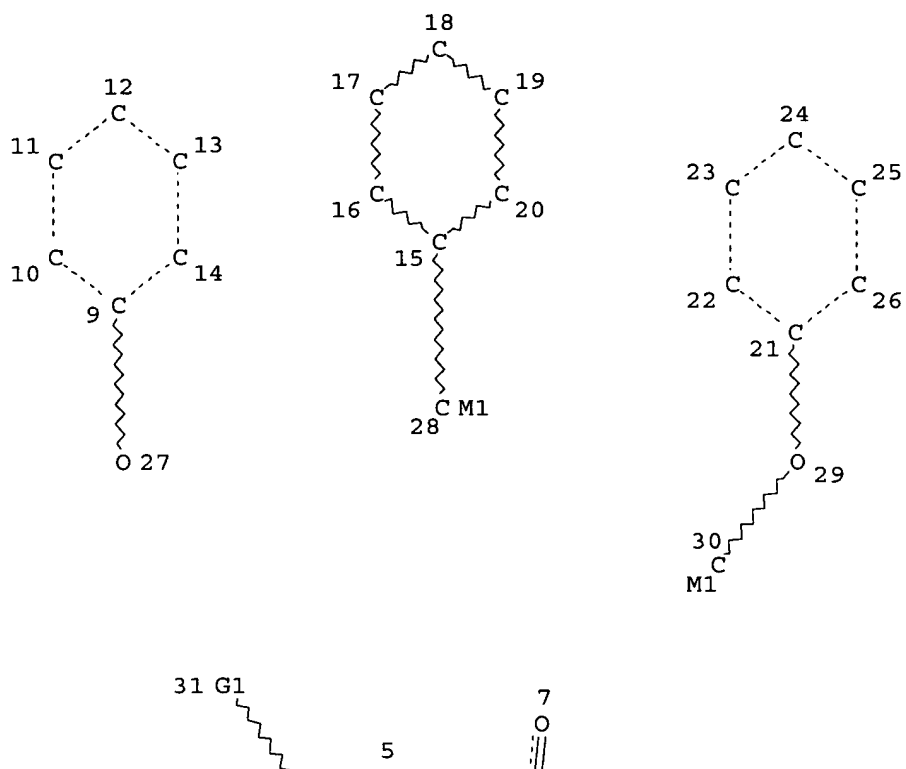
STEREO ATTRIBUTES: NONE

L4 1152 SEA FILE=REGISTRY SSS FUL L1

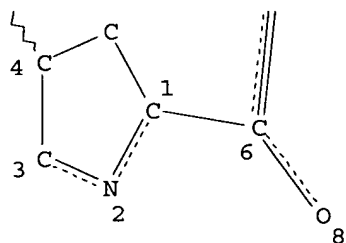
100.0% PROCESSED 17847 ITERATIONS
SEARCH TIME: 00.00.01

1152 ANSWERS

=> d stat que L23
L1 STR



Page 1-A



Page 2-A

VAR G1=27/28/30

NODE ATTRIBUTES:

HCOUNT	IS M1	AT	28
HCOUNT	IS M1	AT	30
NSPEC	IS R	AT	1
NSPEC	IS R	AT	2
NSPEC	IS R	AT	3
NSPEC	IS R	AT	4
NSPEC	IS R	AT	5
NSPEC	IS C	AT	6
NSPEC	IS C	AT	7
NSPEC	IS C	AT	8
NSPEC	IS R	AT	9
NSPEC	IS R	AT	10
NSPEC	IS R	AT	11
NSPEC	IS R	AT	12
NSPEC	IS R	AT	13

NSPEC IS R AT 14
 NSPEC IS R AT 15
 NSPEC IS R AT 16
 NSPEC IS R AT 17
 NSPEC IS R AT 18
 NSPEC IS R AT 19
 NSPEC IS R AT 20
 NSPEC IS R AT 21
 NSPEC IS R AT 22
 NSPEC IS R AT 23
 NSPEC IS R AT 24
 NSPEC IS R AT 25
 NSPEC IS R AT 26
 NSPEC IS C AT 27
 NSPEC IS C AT 28
 NSPEC IS C AT 29
 NSPEC IS C AT 30
 NSPEC IS C AT 31
 DEFAULT MLEVEL IS ATOM
 MLEVEL IS CLASS AT 6 7 8 27 28 29 30
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

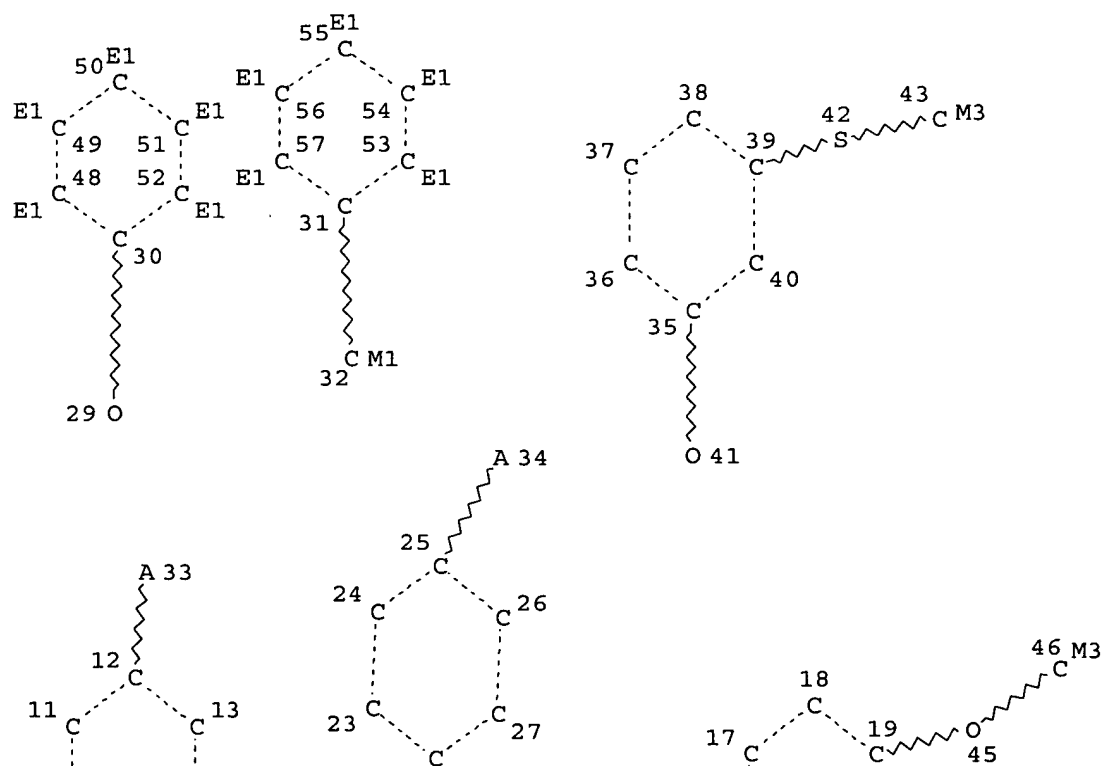
RSPEC 1

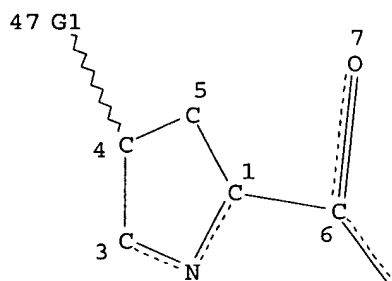
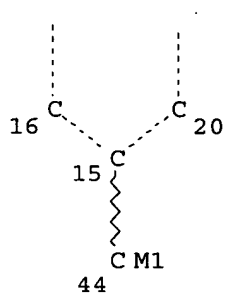
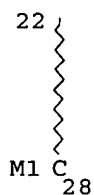
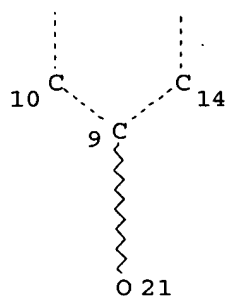
NUMBER OF NODES IS 31

STEREO ATTRIBUTES: NONE

L4 1152 SEA FILE=REGISTRY SSS FUL L1

L20 STR





Page 2-A

2



Page 3-A

VAR G1=21/44/28/29/32/41

NODE ATTRIBUTES:

HCOUNT	IS	M1	AT	28
HCOUNT	IS	M1	AT	32
HCOUNT	IS	M3	AT	43
HCOUNT	IS	M1	AT	44
HCOUNT	IS	M3	AT	46
HCOUNT	IS	E1	AT	48
HCOUNT	IS	E1	AT	49
HCOUNT	IS	E1	AT	50
HCOUNT	IS	E1	AT	51
HCOUNT	IS	E1	AT	52
HCOUNT	IS	E1	AT	53
HCOUNT	IS	E1	AT	54
HCOUNT	IS	E1	AT	55
HCOUNT	IS	E1	AT	56
HCOUNT	IS	E1	AT	57
NSPEC	IS	R	AT	1
NSPEC	IS	R	AT	2
NSPEC	IS	R	AT	3
NSPEC	IS	R	AT	4
NSPEC	IS	R	AT	5
NSPEC	IS	C	AT	6

NSPEC	IS	C	AT	7	
NSPEC	IS	C	AT	8	
NSPEC	IS	R	AT	9	
NSPEC	IS	R	AT	10	
NSPEC	IS	R	AT	11	
NSPEC	IS	R	AT	12	
NSPEC	IS	R	AT	13	
NSPEC	IS	R	AT	14	
NSPEC	IS	R	AT	15	
NSPEC	IS	R	AT	16	
NSPEC	IS	R	AT	17	
NSPEC	IS	R	AT	18	
NSPEC	IS	R	AT	19	
NSPEC	IS	R	AT	20	
NSPEC	IS	C	AT	21	
NSPEC	IS	R	AT	22	
NSPEC	IS	R	AT	23	
NSPEC	IS	R	AT	24	
NSPEC	IS	R	AT	25	
NSPEC	IS	R	AT	26	
NSPEC	IS	R	AT	27	
NSPEC	IS	C	AT	28	
NSPEC	IS	C	AT	29	
NSPEC	IS	R	AT	30	
NSPEC	IS	R	AT	31	
NSPEC	IS	C	AT	32	
NSPEC	IS	RC	AT	33	
NSPEC	IS	RC	AT	34	
NSPEC	IS	R	AT	35	
NSPEC	IS	R	AT	36	
NSPEC	IS	R	AT	37	
NSPEC	IS	R	AT	38	
NSPEC	IS	R	AT	39	
NSPEC	IS	R	AT	40	
NSPEC	IS	C	AT	41	
NSPEC	IS	C	AT	42	
NSPEC	IS	C	AT	43	
NSPEC	IS	C	AT	44	
NSPEC	IS	C	AT	45	
NSPEC	IS	C	AT	46	
NSPEC	IS	C	AT	47	
NSPEC	IS	R	AT	48	
NSPEC	IS	R	AT	49	
NSPEC	IS	R	AT	50	
NSPEC	IS	R	AT	51	
NSPEC	IS	R	AT	52	
NSPEC	IS	R	AT	53	
NSPEC	IS	R	AT	54	
NSPEC	IS	R	AT	55	
NSPEC	IS	R	AT	56	
NSPEC	IS	R	AT	57	
CONNECT	IS	E2	RC	AT	10
CONNECT	IS	E2	RC	AT	11
CONNECT	IS	E2	RC	AT	13
CONNECT	IS	E2	RC	AT	14
CONNECT	IS	E2	RC	AT	16
CONNECT	IS	E2	RC	AT	17
CONNECT	IS	E2	RC	AT	18
CONNECT	IS	E2	RC	AT	20
CONNECT	IS	E2	RC	AT	23

CONNECT IS E2 RC AT 24
CONNECT IS E2 RC AT 26
CONNECT IS E2 RC AT 27
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MLEVEL IS CLASS AT 6 7 8 21 28 29 30 31 32 33 34 41 42 43 44 45 46
48 49 50 51 52 53 54 55 56 57
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 1 30 31
NUMBER OF NODES IS 57

STEREO ATTRIBUTES: NONE

L22 820 SEA FILE=REGISTRY SUB=L4 SSS FUL L20
L23 332 SEA FILE=REGISTRY ABB=ON PLU=ON L4 NOT L22

← structures excluded
by claim 9

=> => file caplus

FILE 'CAPLUS' ENTERED AT 11:44:56 ON 10 MAR 2006

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AUTHOR SEARCH

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FILE COVERS 1907 - 10 Mar 2006 VOL 144 ISS 12
FILE LAST UPDATED: 9 Mar 2006 (20060309/ED)

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<http://www.cas.org/infopolicy.html>

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que nos L31

L27 101 SEA FILE=CAPLUS ABB=ON PLU=ON RAWSON D?/AU
L30 38144 SEA FILE=CAPLUS ABB=ON PLU=ON PROLINE/OBI
L31 1 SEA FILE=CAPLUS ABB=ON PLU=ON L27 AND L30

=> d que nos L33

L27 101 SEA FILE=CAPLUS ABB=ON PLU=ON RAWSON D?/AU
L32 754958 SEA FILE=CAPLUS ABB=ON PLU=ON CALCIUM/BI
L33 4 SEA FILE=CAPLUS ABB=ON PLU=ON L27 AND L32

=> d que nos L29

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L20         STR
L22         820 SEA FILE=REGISTRY SUB=L4 SSS FUL L20
L23         332 SEA FILE=REGISTRY ABB=ON PLU=ON L4 NOT L22
L24         71 SEA FILE=CAPLUS ABB=ON PLU=ON L23
L27         101 SEA FILE=CAPLUS ABB=ON PLU=ON RAWSON D?/AU
L29         1 SEA FILE=CAPLUS ABB=ON PLU=ON L27 AND L24

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=> d que nos L35

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L27         101 SEA FILE=CAPLUS ABB=ON PLU=ON RAWSON D?/AU
L34         65985 SEA FILE=CAPLUS ABB=ON PLU=ON PROLINE/BI
L35         1 SEA FILE=CAPLUS ABB=ON PLU=ON L27 AND L34

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=> d que nos L37

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L27         101 SEA FILE=CAPLUS ABB=ON PLU=ON RAWSON D?/AU
L36         86979 SEA FILE=CAPLUS ABB=ON PLU=ON 34/CC
L37         3 SEA FILE=CAPLUS ABB=ON PLU=ON L36 AND L27

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=> d que nos L40

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L38         990634 SEA FILE=CAPLUS ABB=ON PLU=ON 1/CC
L39         348762 SEA FILE=CAPLUS ABB=ON PLU=ON 63/CC
L40         3 SEA FILE=CAPLUS ABB=ON PLU=ON L27 AND (L38 OR L39)

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=> d que nos L44

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 I OR 89302-81-8/BI)

L8 52 SEA FILE=REGISTRY ABB=ON PLU=ON L7 AND L4
 L20 STR
 L22 820 SEA FILE=REGISTRY SUB=L4 SSS FUL L20
 L27 101 SEA FILE=CAPLUS ABB=ON PLU=ON RAWSON D?/AU
 L41 44 SEA FILE=REGISTRY ABB=ON PLU=ON L8 NOT L22
 L42 10 SEA FILE=CAPLUS ABB=ON PLU=ON L41
 L44 1 SEA FILE=CAPLUS ABB=ON PLU=ON L27 AND L42

=> s L44 or L29 or L31 or L33 or L35 or L37 or L40

L45 9 L44 OR L29 OR L31 OR L33 OR L35 OR L37 OR L40

=> d ibib abs hitind hitstr L45 1-9

L45 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1028480 CAPLUS

DOCUMENT NUMBER: 144:3534

TITLE: The effect of external medium composition on membrane
 water permeability of zebrafish (Danio rerio) embryos
 AUTHOR(S): Adams, Serean L.; Zhang, Tiantian; **Rawson, David**
M.

CORPORATE SOURCE: Luton Institute of Research in the Applied Natural
 Science, University of Luton, Luton, LU1 5DU, UK

SOURCE: Theriogenology (2005), 64(7), 1591-1602

CODEN: THGNBO; ISSN: 0093-691X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of external medium composition on chorion and plasma membrane permeability of zebrafish (Danio rerio) embryos was investigated in this study. Initially, survival of embryos spawned into varying strengths (10-40%) of Hank's solution (HBSS) was assessed. Development and hatching rates for embryos spawned into 30% and 40% HBSS were significantly lower than those obtained with embryos spawned into system water. The effect of embryo survival in 30% HBSS with different **calcium** levels was then investigated. Embryo survival in **calcium** free 30% HBSS or 30% HBSS with 10+ the standard **calcium** concentration was similar to survival in standard 30% HBSS. Membrane water permeability was determined by measuring the floatation time of embryos in test solns. made up with heavy water (D2O) instead of deionized water. Intact embryos at early developmental stages were less permeable than later stages irresp. of the external medium that they were spawned into. In system water, the floatation time of embryos at one-cell and two-cell stages were 1323 and 1189 s, resp., compared to 432 and 353 s at the high and 50% epiboly stages. Change of external medium composition had no effect on membrane permeability of intact embryos at early developmental stages. However, at later stages embryos spawned into 30% HBSS were less permeable than embryos spawned into system water, irresp. of **calcium** concentration. The floatation time of embryos at the high stage increased from 432 s in system water to 468 s in 30% HBSS. The study on dechorionated embryos showed that change of external medium composition had no effect on plasma membrane permeability.

CC 12-3 (Nonmammalian Biochemistry)
ST chorion plasma membrane water permeability embryo medium zebrafish Danio;
osmotic pressure medium water permeability membrane embryo zebrafish;
calcium Hanks soln embryo survival development zebrafish
IT 10043-52-4, **Calcium** chloride, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium** chloride effects on survival and development of
zebrafish embryos spawned into Hank's solution)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1001432 CAPLUS
DOCUMENT NUMBER: 142:86284
TITLE: The design and synthesis of a novel, orally active,
selective ETA antagonist
AUTHOR(S): ~~Rawson, David J.~~; Dack, Kevin N.; Dickinson,
Roger P.; James, Kim; Long, Clive; Walker, Don
CORPORATE SOURCE: Department of Discovery Chemistry, Pfizer Central
Research, Sandwich, CT13 9NJ, UK
SOURCE: Medicinal Chemistry Research (2004), 13(3/4), 149-157
CODEN: MCREEB; ISSN: 1054-2523
PUBLISHER: Birkhaeuser Boston
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The potency and pharmacokinetic properties of an indole-based series of
endothelin antagonists have been optimized using in vitro, in silico and
in vivo methods. Compound 8 is oxidised in vivo to the active metabolite 7
and has been highlighted as an orally active agent suitable for further
profiling. A synthesis of the active enantiomer of the lead compound (8a)
and its metabolite (7a) has been developed and the pharmacokinetic and
pharmacol. profiles of 8a are presented.

CC 1-8 (Pharmacology)
Section cross-reference(s): 28
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:387258 CAPLUS
DOCUMENT NUMBER: 140:391492
TITLE: **Proline** derivatives having affinity for the
calcium channel α -2- δ subunit
INVENTOR(S): ~~Rawson, David James~~
PATENT ASSIGNEE(S): Pfizer Limited, Guinea; Pfizer Inc.
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039367	A1	20040513	WO 2003-IB4697	20031022
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

applicant's
priority
data

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

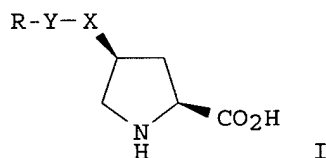
CA 2499698	AA	20040513	CA 2003-2499698	20031022
AU 2003269411	A1	20040525	AU 2003-269411	20031022
EP 1558246	A1	20050803	EP 2003-751192	20031022

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR 2003015839	A	20050927	BR 2003-15839	20031022
US 2004132801	A1	20040708	US 2003-698354	20031030
NL 1024677	A1	20040506	NL 2003-1024677	20031031
NL 1024677	C2	20050704		
NO 2005001407	A	20050726	NO 2005-1407	20050317

PRIORITY APPLN. INFO.: GB 2002-25379 A 20021031
US 2002-428630P P 20021122
WO 2003-IB4697 W 20031022

OTHER SOURCE(S): MARPAT 140:391492
GI



AB The invention describes **proline** derivs. I [X is O, S, NH or CH₂ and Y is CH₂ or a direct bond or Y is O, S or NH and X is CH₂; R is (un)substituted 3-12 membered cycloalkyl, 4-12 membered heterocycloalkyl, aryl or heteroaryl] or their pharmaceutically-acceptable salt, solvates or prodrugs for the treatment of epilepsy, faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain, fibromyalgia, arthritis, neuropathological disorders, sleep disorders, visceral pain disorders and gastrointestinal disorders. Thus, (2S,4S)-4-(benzylthio)pyrrolidine-2-carboxylic acid was prepared from (2S,4R)-4-hydroxypyrrolidine-1,2-dicarboxylic acid di-tert-Bu ester by tosylation, substitution reaction with benzyl mercaptan, and deprotection with TFA.

IC ICM A61K031-401
ICS C07D207-16; C07D401-12; A61P025-00

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63

ST **proline** deriv prepn pharmaceutical

IT Bladder, disease
Inflammation
(cystitis; preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT Nervous system, disease
(degeneration; preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT Mental and behavioral disorders
(depression; preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT Crania
(disorders; preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT Intestine, disease
(inflammatory; preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT Intestine, disease
(irritable bowel syndrome; preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT Dysmenorrhea
(pain; preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT Inflammation
Pancreas, disease
(pancreatitis; preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT Anxiety
(panic; preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT Antiarthritics
Anticonvulsants
Antidepressants
Antirheumatic agents
Anxiety
Anxiolytics
Epilepsy
Hypokinesia
Intestine, disease
Osteoarthritis
Pain
Rheumatoid arthritis
Sleep disorders
(preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT Brain, disease
(syncope; preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT **Calcium** channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α -2- δ subunit; preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT 58632-55-6P 83624-62-8P 105107-84-4P 686766-25-6P 686766-26-7P
686766-27-8P 686766-28-9P 686766-29-0P
686766-30-3P 686766-31-4P 686766-32-5P
686766-33-6P 686766-34-7P 686766-35-8P
686766-36-9P 686766-37-0P 686766-38-1P
686766-39-2P 686766-40-5P 686766-41-6P
686766-42-7P 686766-43-8P 686766-44-9P
686766-87-0P 688007-58-1P 688007-59-2P
688007-60-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **proline** derivs. having affinity for **calcium** channel α -2- δ subunit)

IT 100-39-0, Benzyl bromide 100-53-8, Benzyl mercaptan 106-48-9, 4
Chlorophenol 106-53-6, 4 Bromothiophenol 108-42-9, 3 Chloroaniline
108-43-0, 3 Chlorophenol 367-12-4, 2 Fluorophenol 372-20-3, 3
Fluorophenol 622-95-7, 4 Chlorobenzyl bromide 2216-51-5 23681-89-2
72311-12-7 74844-91-0 88043-21-4 89302-81-8 102195-80-2
159418-27-6 159418-50-5 163190-46-3 170850-75-6 227935-38-8
344286-69-7 686766-86-9
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of **proline** derivs. having affinity for
calcium channel α -2- δ subunit)

IT 54631-82-2P 83623-88-5P 163190-47-4P 262843-21-0P 356558-26-4P
487048-23-7P 686766-45-0P 686766-46-1P 686766-47-2P 686766-48-3P
686766-49-4P 686766-50-7P **686766-51-8P 686766-52-9P**
686766-53-0P **686766-54-1P 686766-55-2P**
686766-56-3P 686766-57-4P 686766-58-5P
686766-59-6P 686766-60-9P 686766-61-0P
686766-62-1P 686766-63-2P **686766-64-3P**
686766-65-4P 686766-66-5P 686766-67-6P
686766-68-7P **686766-69-8P 686766-70-1P**
686766-71-2P 686766-72-3P 686766-73-4P
686766-74-5P 686766-75-6P 686766-76-7P
686766-77-8P 686766-78-9P 686766-79-0P 686766-80-3P
686766-81-4P 686766-82-5P **686766-84-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of **proline** derivs. having affinity for
calcium channel α -2- δ subunit)

IT **686766-27-8P 686766-29-0P 686766-30-3P**
686766-31-4P 686766-32-5P 686766-33-6P
686766-34-7P 686766-36-9P 686766-37-0P
686766-38-1P 686766-39-2P 686766-40-5P
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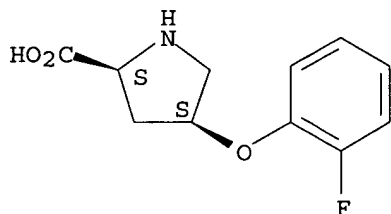
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of **proline** derivs. having affinity for
calcium channel α -2- δ subunit)

RN 686766-27-8 CAPLUS

CN L-Proline, 4-(2-fluorophenoxy)-, (4S)- (9CI) (CA INDEX NAME)

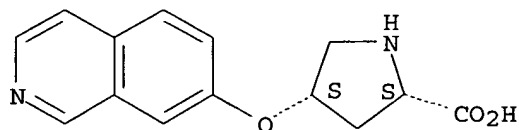
Absolute stereochemistry.



RN 686766-29-0 CAPLUS

CN L-Proline, 4-(7-isoquinolinyloxy)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

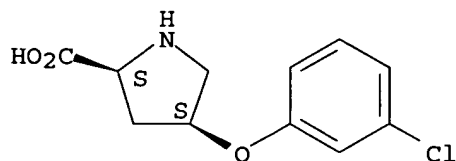


RN 686766-30-3 CAPLUS

CN L-Proline, 4-(3-chlorophenoxy)-, hydrochloride, (4S)- (9CI) (CA INDEX NAME)

NAME)

Absolute stereochemistry.

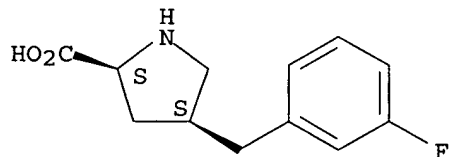


● HCl

RN 686766-31-4 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, hydrochloride, (4S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

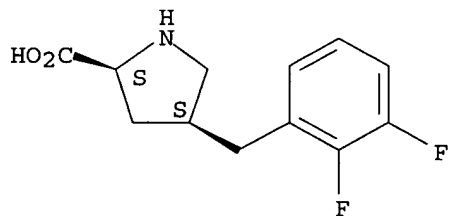


● HCl

RN 686766-32-5 CAPLUS

CN L-Proline, 4-[(2,3-difluorophenyl)methyl]-, hydrochloride, (4S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

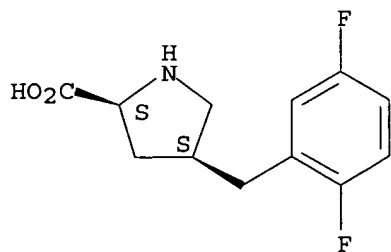


● HCl

RN 686766-33-6 CAPLUS

CN L-Proline, 4-[(2,5-difluorophenyl)methyl]-, hydrochloride, (4S) - (9CI) (CA INDEX NAME)

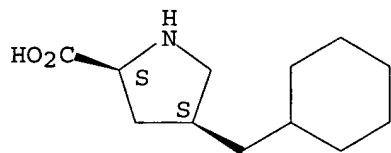
Absolute stereochemistry. Rotation (-).



● HCl

RN 686766-34-7 CAPLUS
CN L-Proline, 4-(cyclohexylmethyl)-, hydrochloride, (4S)- (9CI) (CA INDEX NAME)

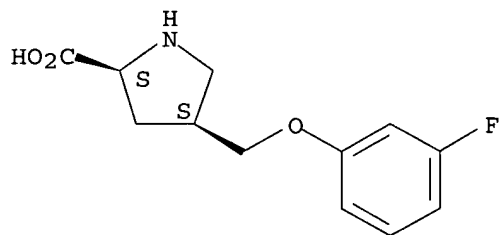
Absolute stereochemistry. Rotation (-).



● HCl

RN 686766-36-9 CAPLUS
CN L-Proline, 4-[(3-fluorophenoxy)methyl]-, hydrochloride, (4S)- (9CI) (CA INDEX NAME)

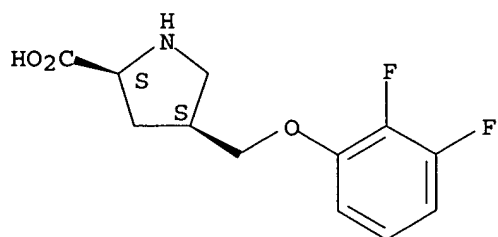
Absolute stereochemistry.



● HCl

RN 686766-37-0 CAPLUS
CN L-Proline, 4-[(2,3-difluorophenoxy)methyl]-, (4S)- (9CI) (CA INDEX NAME)

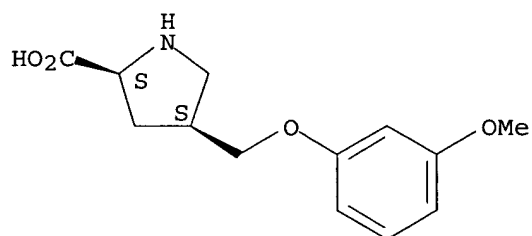
Absolute stereochemistry.



RN 686766-38-1 CAPLUS

CN L-Proline, 4-[(3-methoxyphenoxy)methyl]-, (4S)-(9CI) (CA INDEX NAME)

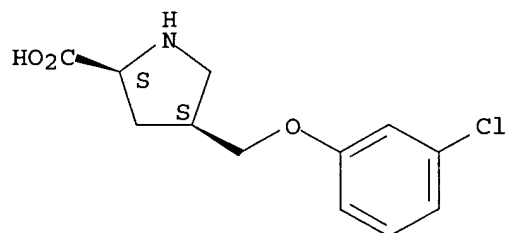
Absolute stereochemistry.



RN 686766-39-2 CAPLUS

CN L-Proline, 4-[(3-chlorophenoxy)methyl]-, hydrochloride, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

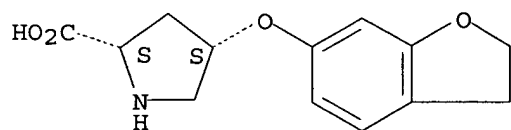


● HCl

RN 686766-40-5 CAPLUS

CN L-Proline, 4-[(2,3-dihydro-6-benzofuranyl)oxy]-, hydrochloride, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

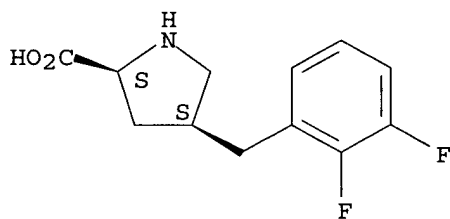


● HCl

RN 686766-42-7 CAPLUS

CN L-Proline, 4-[(2,3-difluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

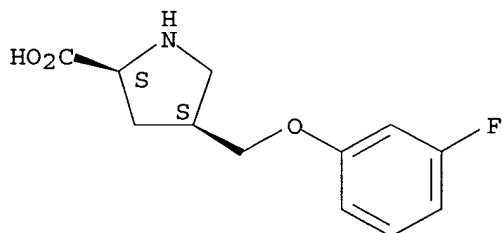
Absolute stereochemistry.



RN 686766-43-8 CAPLUS

CN L-Proline, 4-[(3-fluorophenoxy)methyl]-, (4S)- (9CI) (CA INDEX NAME)

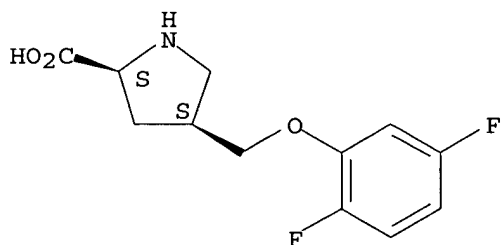
Absolute stereochemistry.



RN 686766-44-9 CAPLUS

CN L-Proline, 4-[(2,5-difluorophenoxy)methyl]-, (4S)- (9CI) (CA INDEX NAME)

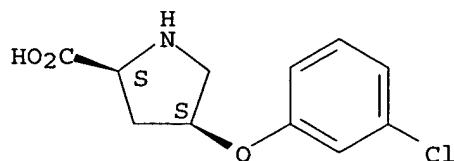
Absolute stereochemistry.



RN 686766-87-0 CAPLUS

CN L-Proline, 4-(3-chlorophenoxy)-, (4S)- (9CI) (CA INDEX NAME)

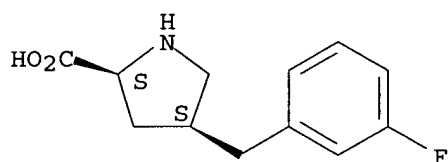
Absolute stereochemistry.



RN 688007-58-1 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

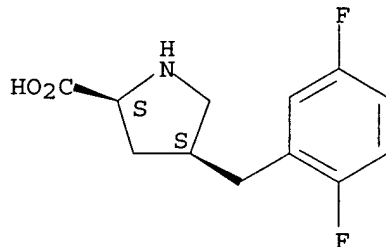
Absolute stereochemistry.



RN 688007-59-2 CAPLUS

CN L-Proline, 4-[(2,5-difluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

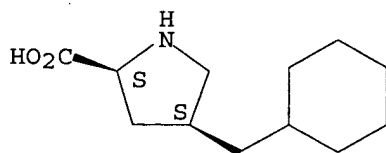
Absolute stereochemistry. Rotation (-).



RN 688007-60-5 CAPLUS

CN L-Proline, 4-(cyclohexylmethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 686766-51-8P 686766-52-9P 686766-54-1P
686766-55-2P 686766-56-3P 686766-57-4P
686766-58-5P 686766-59-6P 686766-60-9P
686766-61-0P 686766-62-1P 686766-64-3P
686766-65-4P 686766-66-5P 686766-67-6P
686766-69-8P 686766-70-1P 686766-71-2P

686766-72-3P 686766-74-5P 686766-75-6P
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 686766-84-7P

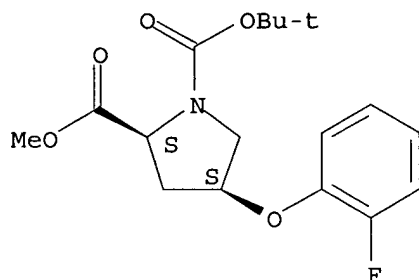
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation of **proline** derivs. having affinity for
calcium channel α -2- δ subunit)

RN 686766-51-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-fluorophenoxy)-,
 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

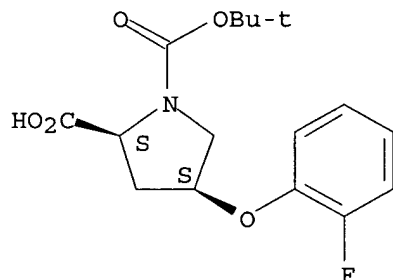
Absolute stereochemistry.



RN 686766-52-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-fluorophenoxy)-,
 1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

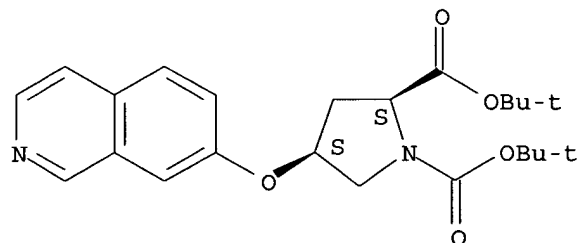
Absolute stereochemistry.



RN 686766-54-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(7-isoquinolinyloxy)-,
 bis(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

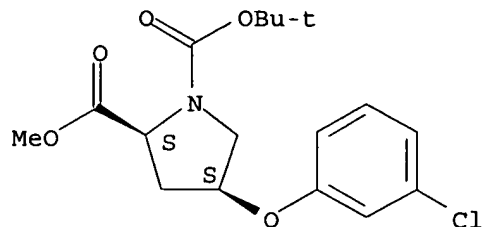
Absolute stereochemistry.



RN 686766-55-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3-chlorophenoxy)-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

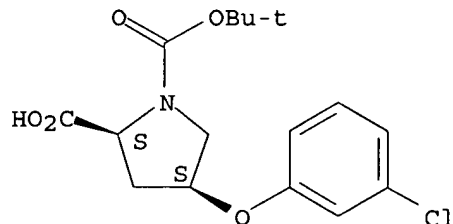
Absolute stereochemistry.



RN 686766-56-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3-chlorophenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

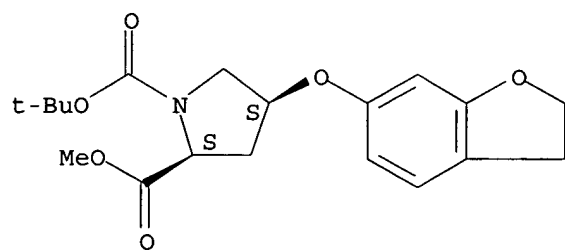
Absolute stereochemistry.



RN 686766-57-4 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,3-dihydro-6-benzofuranyl)oxy]-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

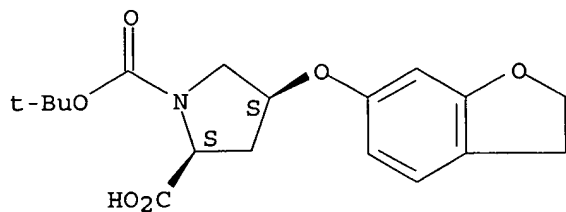
Absolute stereochemistry.



RN 686766-58-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,3-dihydro-6-benzofuranyl)oxy]-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

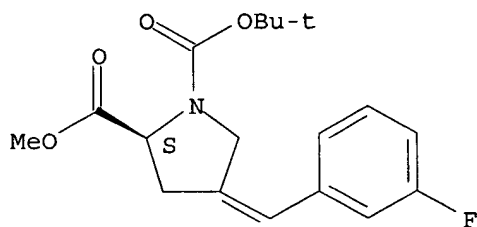
Absolute stereochemistry.



RN 686766-59-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methylene]-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S)- (9CI) (CA INDEX NAME)

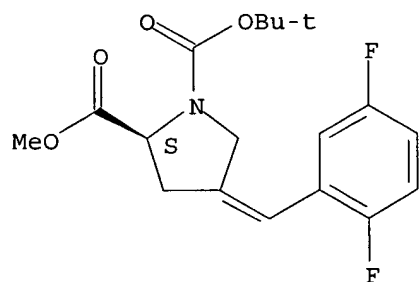
Absolute stereochemistry.
Double bond geometry unknown.



RN 686766-60-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,5-difluorophenyl)methylene]-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S)- (9CI) (CA INDEX NAME)

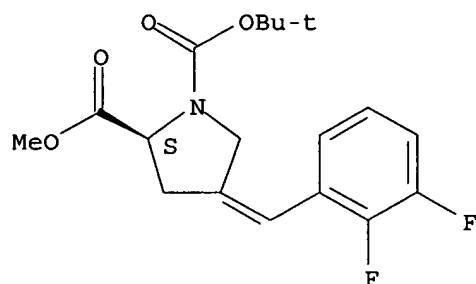
Absolute stereochemistry.
Double bond geometry unknown.



RN 686766-61-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,3-difluorophenyl)methylene]-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S)- (9CI) (CA INDEX NAME)

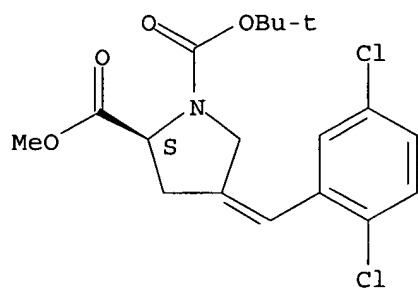
Absolute stereochemistry.
Double bond geometry unknown.



RN 686766-62-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,5-dichlorophenyl)methylene]-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S)- (9CI) (CA INDEX NAME)

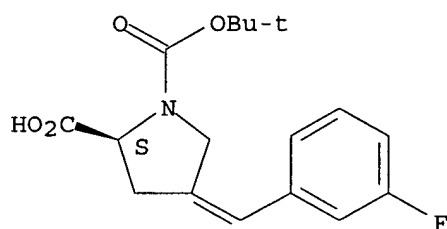
Absolute stereochemistry.
Double bond geometry unknown.



RN 686766-64-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methylene]-, 1-(1,1-dimethylethyl) ester, (2S)- (9CI) (CA INDEX NAME)

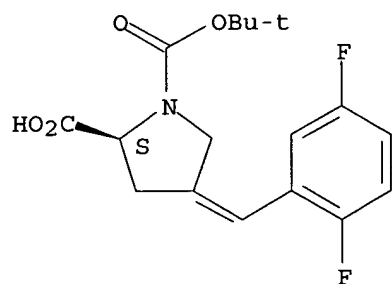
Absolute stereochemistry.
Double bond geometry unknown.



RN 686766-65-4 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,5-difluorophenyl)methylene]-, 1-(1,1-dimethylethyl) ester, (2S)- (9CI) (CA INDEX NAME)

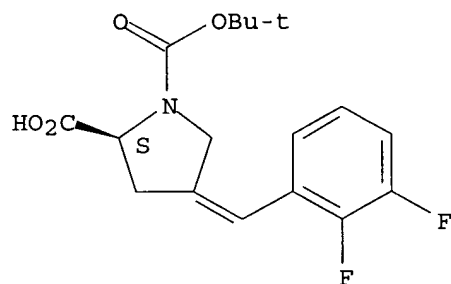
Absolute stereochemistry.
Double bond geometry unknown.



RN 686766-66-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,3-difluorophenyl)methylene]-, 1-(1,1-dimethylethyl) ester, (2S)- (9CI) (CA INDEX NAME)

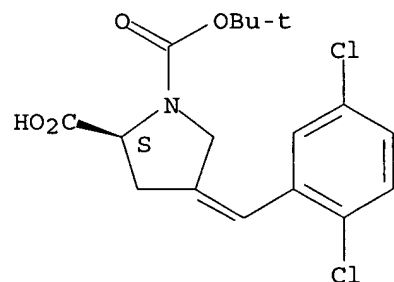
Absolute stereochemistry.
Double bond geometry unknown.



RN 686766-67-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,5-dichlorophenyl)methylene]-, 1-(1,1-dimethylethyl) ester, (2S)- (9CI) (CA INDEX NAME)

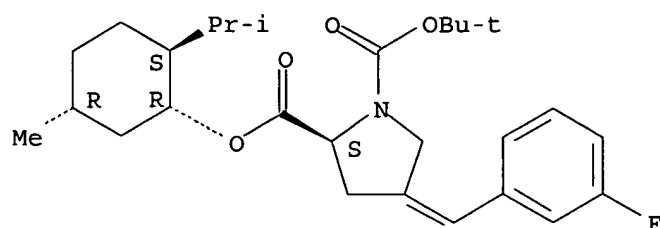
Absolute stereochemistry.
Double bond geometry unknown.



RN 686766-69-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methylene]-, 1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl] ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

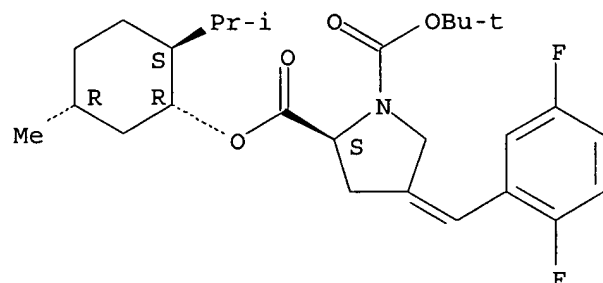


RN 686766-70-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,5-difluorophenyl)methylene]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

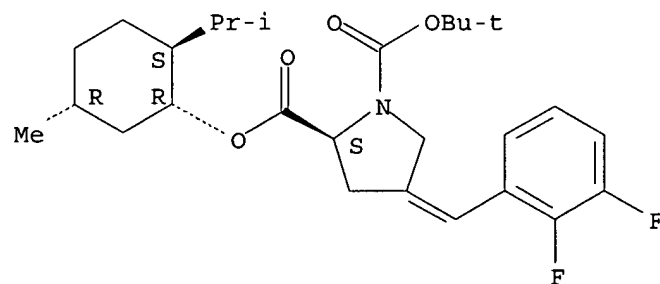


RN 686766-71-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,3-difluorophenyl)methylene]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

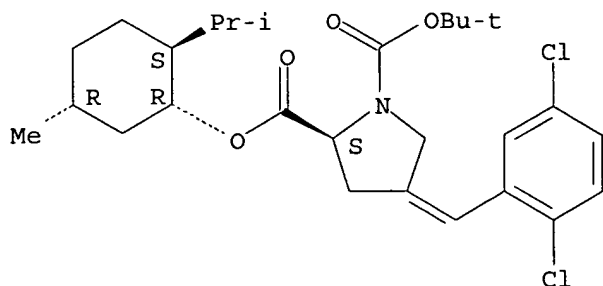


RN 686766-72-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,5-dichlorophenyl)methylene]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

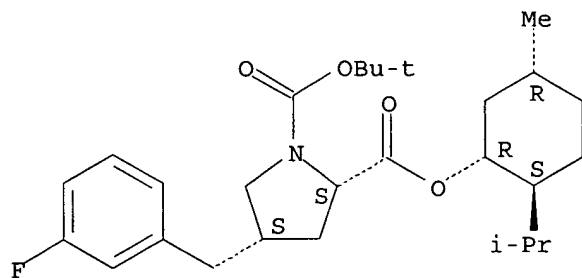
Double bond geometry unknown.



RN 686766-74-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methyl]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S,4S)- (9CI) (CA INDEX NAME)

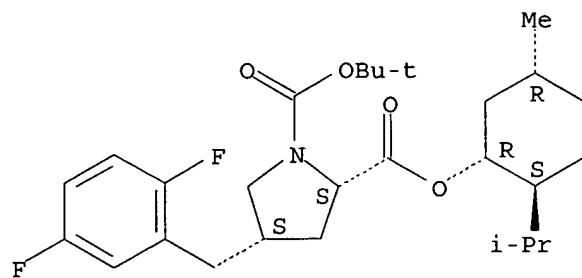
Absolute stereochemistry.



RN 686766-75-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,5-difluorophenyl)methyl]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S,4S)- (9CI) (CA INDEX NAME)

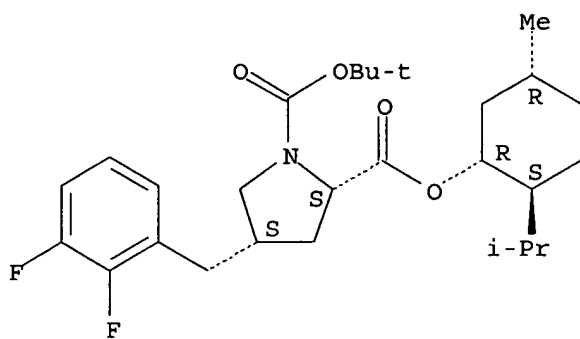
Absolute stereochemistry.



RN 686766-76-7 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,3-difluorophenyl)methyl]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S,4S)- (9CI) (CA INDEX NAME)

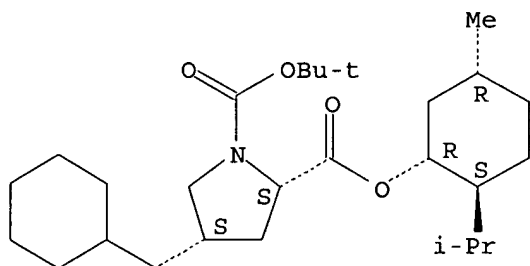
Absolute stereochemistry. Rotation (-).



RN 686766-77-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(cyclohexylmethyl)-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S,4S)- (9CI) (CA INDEX NAME)

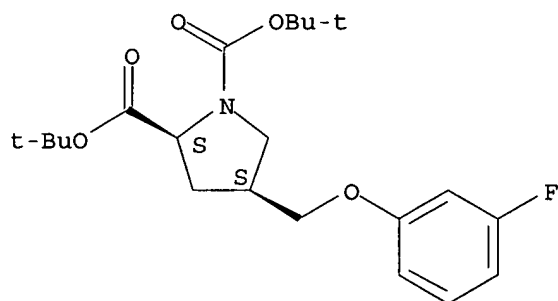
Absolute stereochemistry.



RN 686766-81-4 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenoxy)methyl]-,
bis(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

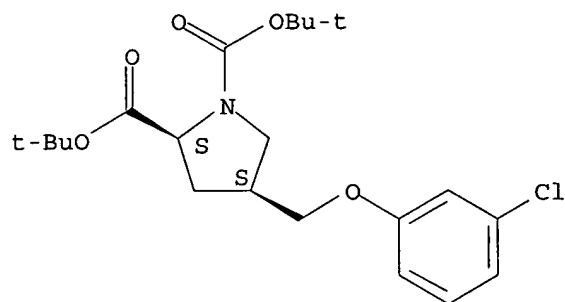
Absolute stereochemistry.



RN 686766-84-7 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-chlorophenoxy)methyl]-,
bis(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:162663 CAPLUS

DOCUMENT NUMBER: 140:199744

TITLE: Preparation of substituted glycine derivatives for use as medicaments

INVENTOR(S): Blakemore, David Clive; Bryans, Justin Stephan; Maw, Graham Nigel; **Rawson, David James**; Thompson, Lisa Rosemary; Chu, Wai-lam Alexis

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

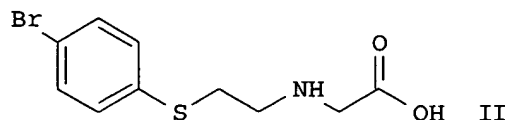
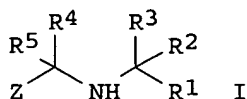
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004016583	A1	20040226	WO 2003-IB3708	20030804
WO 2004016583	C1	20040527		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2494546	AA	20040226	CA 2003-2494546	20030804
AU 2003255954	A1	20040303	AU 2003-255954	20030804
EP 1539687	A1	20050615	EP 2003-787971	20030804
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013527	A	20050628	BR 2003-13527	20030804
JP 2005535716	T2	20051124	JP 2004-528767	20030804
US 2004092498	A1	20040513	US 2003-640520	20030813
PRIORITY APPLN. INFO.:				
			GB 2002-19153	A 20020816
			US 2002-413856P	P 20020925
			WO 2003-IB3708	W 20030804

OTHER SOURCE(S): MARPAT 140:199744

GI



proline derivatives?

AB The title compound I [R1 = hydroxycarbonyl, a carboxylic acid biostere, or prodrug; R2, R3, R4, R5 = H, alkyl, alkoxyalkyl; Z = a C-linked 5-membered heterocycloalkyl or heteroaryl substituted with alkyl or fused with cycloalkyl, heterocycloalkyl, Ph, or monocyclic heteroaryl, etc., or Z = R8XYCR6R7-, wherein R6, R7 = H, alkyl, alkoxyalkyl; R8 = alkyl, cycloalkyl, heterocycloalkyl, aryl, etc.; Y = S, O, CH2, or NH and X = absence or (substituted)C1-C2 alkyl; or X = S, O, CH2, or NH and Y = (substituted)C1-C2 alkyl] were prepared in the treatment of epilepsy, faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain, arthritis, neuropathol. disorders, sleep disorders, visceral pain disorders and gastrointestinal disorders. Thus, reaction of tert-butyl(2-oxo-1,3-oxazolidin-3-yl)acetate with 4-bromothiophenol followed by hydrolysis yielded compound II. The latter showed a binding affinity of 59 nM in the radioligand binding assay.

IC ICM C07C323-25

ICS C07C229-12; C07D217-02; C07C323-32; C07C229-14; A61K031-198; A61K031-223; A61K031-47

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:779804 CAPLUS

DOCUMENT NUMBER: 136:112215

TITLE: Absorption, distribution, metabolism, and excretion considerations in selection of orally active indole-containing endothelin antagonist

AUTHOR(S): Walker, Donald K.; Dack, Kevin N.; Dickinson, Roger P.; Fenner, Katherine S.; James, Kim; **Rawson, David J.**; Smith, Dennis A.

CORPORATE SOURCE: Department of Drug Metabolism, Pfizer Global Research and Development, Sandwich, CT13 9NJ, UK

SOURCE: Drug Metabolism and Disposition (2001), 29(11), 1424-1431

CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of potent indole-containing endothelin antagonists were evaluated in rat pharmacokinetic studies as part of a rational drug design program. Early compds. in this series were found to show poor gastrointestinal

absorption, limiting their utility as oral agents. Structural modifications and pharmacokinetic studies indicated that reducing the overall H-bonding potential, through a reduction in the number of H-bond donors and acceptors, could increase absorption of the mols. There was a correlation between calculated H-bonding capacity and rate of permeability across Caco-2 monolayers for this series of compds. Caco-2 permeability was also shown to be indicative of the estimated extent of absorption in rats. Balancing the requirements of absorption and systemic clearance lead to the selection of an alc.-containing compound, compound 7a (single enantiomer of compound 7) that was moderately absorbed after oral administration and converted to an active acid metabolite, which itself was of low intrinsic clearance. Species differences were observed between the absorption of compound 7a in rat and dog and also in the extent of conversion to the acid metabolite. Absorption was estimated at 30% in rat and 100% in dog. Approx. 30% of the absorbed drug was converted to systemically available acid metabolite in rat, compared with only 3% in dog.

CC 1-3 (Pharmacology)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:784080 CAPLUS

DOCUMENT NUMBER: 130:110585

TITLE: The preparation of enantiomerically enriched γ -amino acids (GABAs) using palladium catalyzed allylic substitution

AUTHOR(S): Martin, Christopher J.; Rawson, David J.; Williams, Jonathan M. J.

CORPORATE SOURCE: Department of Chemistry, Loughborough University, Loughborough/Leicestershire, LE11 3TU, UK

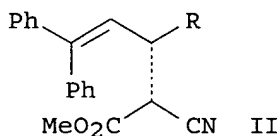
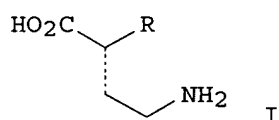
SOURCE: Tetrahedron: Asymmetry (1998), 9(20), 3723-3730
CODEN: TASYE3; ISSN: 0957-4166

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB Enantioselective, palladium-catalyzed allylic substitution reaction was used as the asymmetry-producing step in the synthesis of enantiomerically enriched γ -amino acid I (R = Me, Ph). For example, starting material $\text{Ph}_2\text{C}:\text{CHCH}(\text{OAc})\text{R}$ underwent Pd-catalyzed allylic substitution in the presence of 10 mol% of (4S)-4,5-dihydro-4-isopropyl-2-[2-(diphenylphosphino)phenyl]-1,3-oxazole, 2.5 mol% of $[\text{Pd}(\text{allyl})\text{Cl}]_2$, Me cyanoacetate, NaH and THF/DMF at 20° for 36-48 h to give the acetate II. Acetate II was converted to substituted γ -aminobutyric acid I in five steps that included Krapcho decarboxylation, LiAlH_4 reduction, N-protection with benzyl chloroformate, oxidative cleavage with CrO_3 and N-deprotection with H_2 and Pd/C.

CC 34-2 (Amino Acids, Peptides, and Proteins)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:558214 CAPLUS
DOCUMENT NUMBER: 113:158214
TITLE: Whole-cell biosensors for environmental monitoring
AUTHOR(S): **Rawson, David M.**; Willmer, Allison J.;
Turner, Anthony P. F.
CORPORATE SOURCE: Cent. Appl. Technol. Innovation, Luton Coll. Higher
Educ., Luton/Bedfordshire, LU2 8LE, UK
SOURCE: Biosensors (1989) 4(5), 299-311
CODEN: BISSED; ISSN: 0265-928X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A biosensor for use in monitoring herbicides in lowland river water (for the protection of drinking water plant intakes) incorporates alginate-immobilized *Synechococcus*, a cyanobacterium, as the biocatalyst and can detect a wide range of herbicides with sites of action on the photosynthetic electron transport chain at concns. of ≥ 20 $\mu\text{g/L}$ and has a working life of ≤ 7 days. Cyanobacterium entrapped in dehydrated alginate beads had a useful shelf life of 5-10 wks. Immobilization on Al₂O₃ membranes was also studied.

CC 61-2 (Water)

Section cross-reference(s): 4, 5, 11

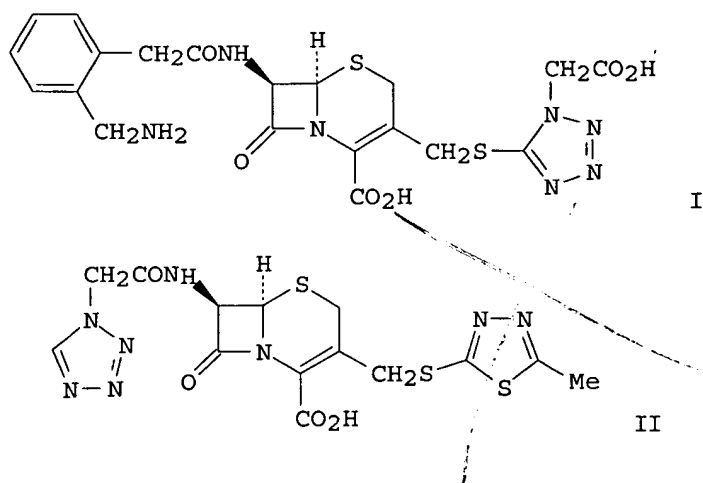
IT 9005-35-0, **Calcium** alginate

RL: OCCU (Occurrence)

(*Synechococcus* immobilized on, for biosensor for herbicide detection in river water)

L45 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1980:461708 CAPLUS
DOCUMENT NUMBER: 93:61708
TITLE: Comparison of ceforanide and cefazolin treatment of bacterial pneumonia
AUTHOR(S): ~~Rawson, Daniel~~; Jones, Donna S.; Crain, Doris; Perlino, Carl A.
CORPORATE SOURCE: Dep. Med., Emory Univ., Atlanta, GA, 30303, USA
SOURCE: Curr. Chemother. Infect. Dis., Proc. Int. Congr. Chemother., 11th (1980), Meeting Date 1979, Volume 1, 450-1. Editor(s) Nelson, John D.; Grassi, Carlo. Am. Soc. Microbiol.: Washington, D. C.
CODEN: 43MKAT
DOCUMENT TYPE: Conference
LANGUAGE: English
GI



AB In human subjects, parenteral ceforanide (I) [60925-61-3] was an effective alternative to cefazolin (II) [25953-19-9] in the treatment of bacterial pneumonia due to *Streptococcus pneumoniae* or *Haemophilus influenzae* and offers the advantage of a 12 h dose schedule (as compared to 8 h with II). I was well tolerated, with few side effects. II produced a higher incidence of liver enzyme abnormalities than has been reported previously. These did not appear to be related to underlying illnesses or the type of bacterial infection.

CC 1-6 (Pharmacodynamics)

L45 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1977:580120 CAPLUS

DOCUMENT NUMBER: 87:180120

TITLE: An improved method for the automated determination of urine **calcium**

AUTHOR(S): Rawson, D. R. W.; Attwood, E. C.

CORPORATE SOURCE: Dep. Clin. Chem., Cty. Hosp., Hereford, UK

SOURCE: Clinical Biochemistry (1977), 10(4), 156-8

CODEN: CLBIAS; ISSN: 0009-9120

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ca was precipitated overnight as the oxalate from urine acidified to pH 4.5; the

precipitate then was dissolved in 0.5M H₂SO₄ and analyzed by using either the AutoAnalyzer I or SMA PLUS and cresolphthalein complexone reagent containing 8-hydroxyquinoline. To eliminate low values, as compared with KMnO₄ manual titration, the Ca stds. used in the automated method were dissolved in 0.5M H₂SO₄. Initial separation of the Ca from the urine and the solution of

stds. in H₂SO₄ resulted in a correlation coefficient of 0.994 between the titration and

the automated method and recoveries of .apprx.98%.

CC 9-4 (Biochemical Methods)

ST urine **calcium** detn; spectrometry automated **calcium**

IT Urine analysis

(**calcium** determination in, automated spectrometric)

=> □

NARROW STRUCTURE SEARCH

=> file caplus

FILE 'CAPLUS' ENTERED AT 11:47:11 ON 10 MAR 2006

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FILE COVERS 1907 - 10 Mar 2006 VOL 144 ISS 12

FILE LAST UPDATED: 9 Mar 2006 (20060309/ED)

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<http://www.cas.org/infopolicy.html>

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que nos L42

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74844-91-0/BI OR 83623-88-5/BI OR 83624-62-8/BI OR 88043-21-4/B
I OR 89302-81-8/BI)

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L20 STR
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L46 9 ((L42 OR L43)) NOT L45

=> d ibib abs hitind hitstr L46 1-9

L46 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1220313 CAPLUS
DOCUMENT NUMBER: 143:478200
TITLE: Preparation of novel proline and morpholine

derivatives as inhibitors of 11- β -hydroxysteroid
dehydrogenase type 1 (11- β -hsd-1) for the
treatment of diabetes and obesity

INVENTOR(S): Cheng, Hengmiao; Smith, Christopher Ronald; Wang,
Yong; Parrott, Timothy James; Dress, Klaus Ruprecht;
Nair, Sajiv Krishnan; Hoffman, Jacqui Elizabeth; Le,
Phuong Thi Quy; Kupchinsky, Stanley William; Yang, Yi;
Cripps, Stephan James; Huang, Buwen
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005108359	A1	20051117	WO 2005-IB1140	20050425
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, <u>US</u> , UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005261290	A1	20051124	US 2005-122599	20050504
PRIORITY APPLN. INFO.:			US 2004-569362P	P 20040506

OTHER SOURCE(S): MARPAT 143:478200

AB The invention relates to compds. of general formula T-CONR₁R₂ [R₁ is
alkyl, cycloalkyl-, aryl- or heterocyclylalkyl; R₂ is H or alkyl; T is 4-
to 10-membered heterocyclyl containing at least one nitrogen atom which is
optionally substituted by at least one R₃ group (R₃ is CF₃, CHF₂, CH₂F,
CF₃O, alkoxy, alkyl, acyl, etc.)] or their pharmaceutically-acceptable
salts and to compns. containing these compds. for treating a condition that is
mediated by modulation of the 11- β -hsd-1 enzyme. Thus,
N-(cyclohexylmethyl)-D-proline benzylamide was prepared from Boc-protected
D-proline by benzylamidation, deprotection, and reaction with
cyclohexylmethyl bromide.

IC ICM C07D207-16
ICS C07D211-60; C07D211-96; C07D265-30; A61K031-401; A61K031-445;
A61K031-5375

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 28, 63

IT 81357-21-3P 92235-33-1P 116774-46-0P 147266-79-3P 149252-59-5P
 177032-44-9P 184871-49-6P 220534-64-5P 449758-61-6P 486415-31-0P
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 869682-24-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of novel proline and morpholine derivs. as inhibitors of 11- β -hydroxysteroid dehydrogenase type 1 (11- β -hsd-1) for treatment of diabetes and obesity)

IT 686766-52-9P 869681-95-8P 869681-96-9P
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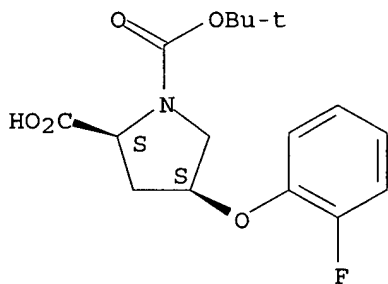
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of novel proline and morpholine derivs. as inhibitors of 11- β -hydroxysteroid dehydrogenase type 1 (11- β -hsd-1) for treatment of diabetes and obesity)

RN 686766-52-9 CAPLUS

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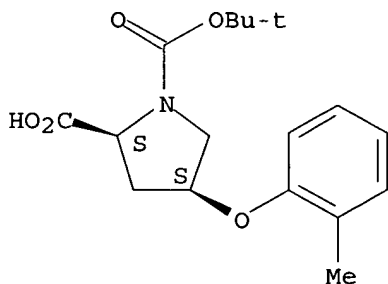
Absolute stereochemistry.



RN 869681-95-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-methylphenoxy)-, 1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

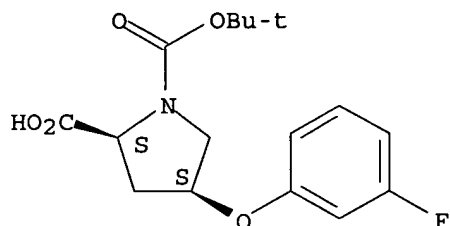
Absolute stereochemistry.



RN 869681-96-9 CAPLUS

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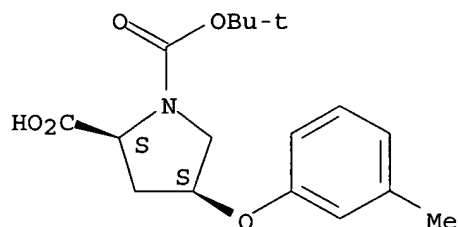
Absolute stereochemistry.



RN 869681-97-0 CAPLUS

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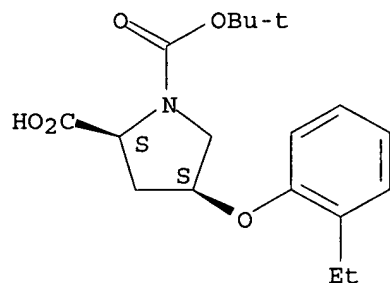
Absolute stereochemistry.



RN 869682-00-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-ethylphenoxy)-,
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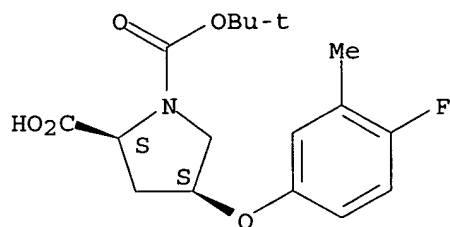
Absolute stereochemistry.



RN 869682-01-9 CAPLUS

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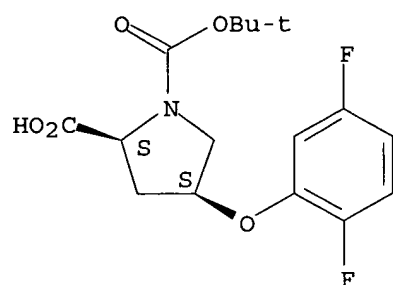
Absolute stereochemistry.



RN 869682-02-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2,5-difluorophenoxy)-,
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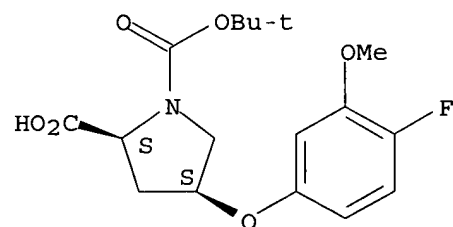
Absolute stereochemistry.



RN 869682-03-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(4-fluoro-3-methoxyphenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

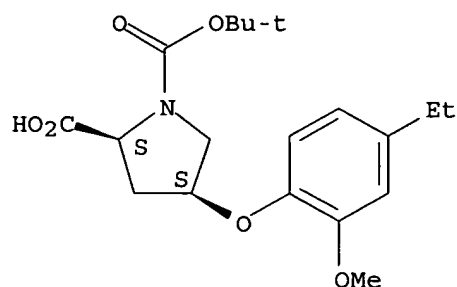
Absolute stereochemistry.



RN 869682-04-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(4-ethyl-2-methoxyphenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

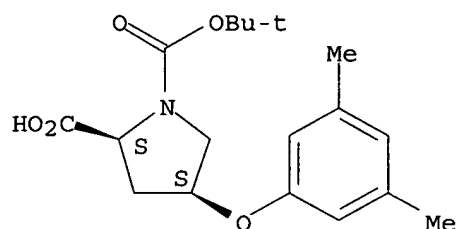
Absolute stereochemistry.



RN 869682-05-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3,5-dimethylphenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

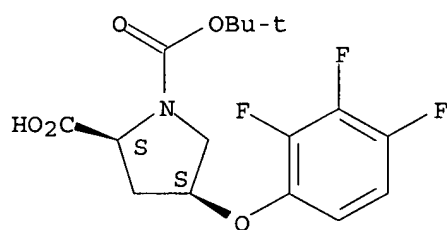
Absolute stereochemistry.



RN 869682-06-4 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2,3,4-trifluorophenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

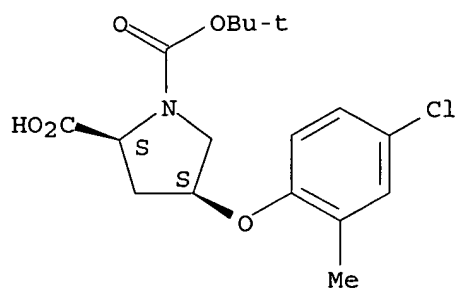
Absolute stereochemistry.



RN 869682-07-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(4-chloro-2-methylphenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

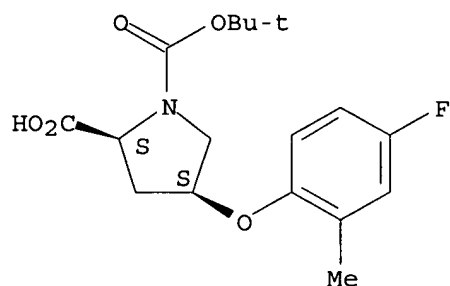
Absolute stereochemistry.



RN 869682-08-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(4-fluoro-2-methylphenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

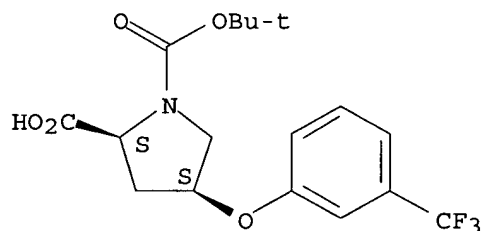
Absolute stereochemistry.



RN 869682-09-7 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[3-(trifluoromethyl)phenoxy]-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

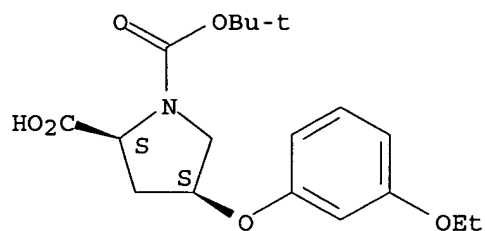
Absolute stereochemistry.



RN 869682-10-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3-ethoxyphenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

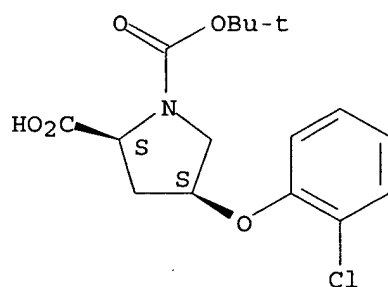
Absolute stereochemistry.



RN 869682-11-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-chlorophenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

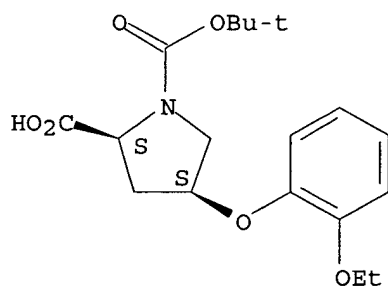
Absolute stereochemistry.



RN 869682-12-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-ethoxyphenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

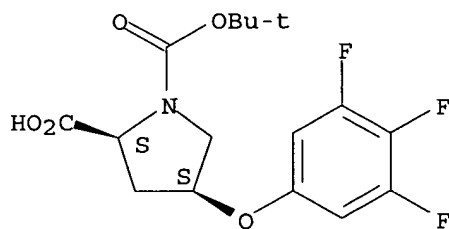
Absolute stereochemistry.



RN 869682-13-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3,4,5-trifluorophenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

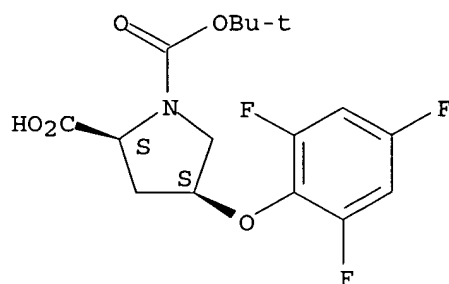
Absolute stereochemistry.



RN 869682-14-4 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2,4,6-trifluorophenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

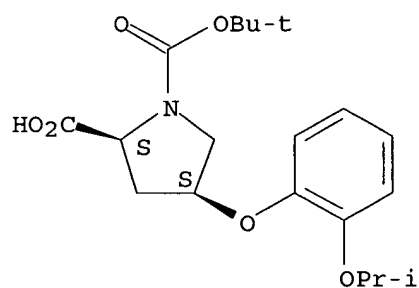
Absolute stereochemistry.



RN 869682-15-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[2-(1-methylethoxy)phenoxy]-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

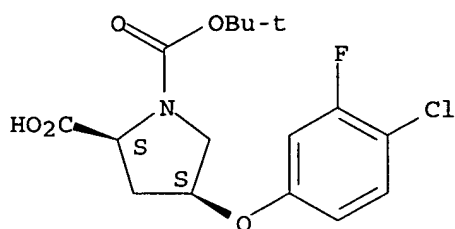
Absolute stereochemistry.



RN 869682-16-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(4-chloro-3-fluorophenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1170963 CAPLUS

DOCUMENT NUMBER: 143:440755

TITLE: Combinations comprising α -2-8 ligands and NMDA receptor antagonists

INVENTOR(S): Hizue, Masanori; Imai, Aki; Toide, Katsuo

PATENT ASSIGNEE(S): Pfizer Japan, Inc., Japan; Pfizer Inc.

SOURCE: PCT Int. Appl., 69 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005102390	A2	20051103	WO 2005-IB988	20050411
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2004-564374P P 20040422

AB The invention relates to a synergistic combination of an α -2-8 ligand and an NMDA receptor antagonist (preferably an NR2B antagonist) or pharmaceutically-acceptable salts, esters or pharmaceutical compns. and their use in the treatment of pain, particularly neuropathic pain, and disorders of the central nervous system. Synthetic examples describe the preparation of α -2-8 ligands, e.g., (3R,4R,5R)-3-amino-4,5-dimethylheptanoic acid, useful in the combinations of the invention. The combination of 3-methylgabapentin as α -2-8 ligand and (-)-(R)-6-[2-[4-(3-fluorophenyl)-4-hydroxy-1-piperidinyl]-1-hydroxyethyl]-3,4-dihydro-2(1H)-quinolinone as NR2B antagonist produced synergy in ability to relieve neuropathic pain.

IC ICM A61K045-06

ICS A61K031-195; A61P029-00

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 63

IT 125-71-3, Dextromethorphan 6740-88-1, Ketamine 19982-08-2, Memantine

23210-56-2, Ifenprodil 60142-96-3, Gabapentin 134234-12-1, Traxoprodil
 148553-50-8, Pregabalin 196608-53-4 202914-18-9, CHF-3381
 223445-75-8 227625-35-6 227626-51-9 313651-33-1 335458-65-6
 473924-33-3 610300-07-7 610300-19-1 610300-20-4 **686766-42-7**
686766-43-8 686766-87-0 688007-58-1
 868561-90-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (combinations comprising α -2- δ ligands and NMDA receptor
 antagonists)

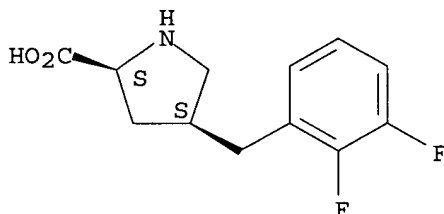
IT **686766-42-7 686766-43-8 686766-87-0**
688007-58-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (combinations comprising α -2- δ ligands and NMDA receptor
 antagonists)

RN 686766-42-7 CAPLUS

CN L-Proline, 4-[(2,3-difluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

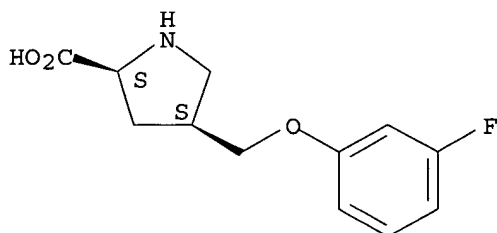
Absolute stereochemistry.



RN 686766-43-8 CAPLUS

CN L-Proline, 4-[(3-fluorophenoxy)methyl]-, (4S)- (9CI) (CA INDEX NAME)

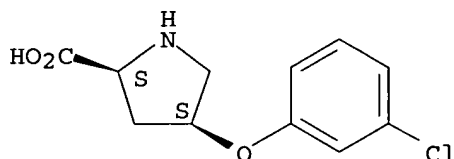
Absolute stereochemistry.



RN 686766-87-0 CAPLUS

CN L-Proline, 4-(3-chlorophenoxy)-, (4S)- (9CI) (CA INDEX NAME)

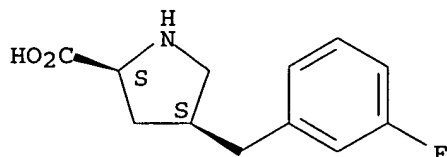
Absolute stereochemistry.



RN 688007-58-1 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L46 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1170698 CAPLUS

DOCUMENT NUMBER: 143:446634

TITLE: Combinations comprising EP4-receptor antagonists and $\alpha 2\delta$ ligands for treating pain

INVENTOR(S): Audoly, Laurent Pascal

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 267 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005102389	A2	20051103	WO 2005-IB935	20050408
W: AE, AG, AL, AM, AT, AU, <u>AE</u> , BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, <u>PL</u> , PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2004-563863P P 20040420

AB The present invention relates to a combination of an EP4-receptor antagonist (e.g. 4-[[[5-fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]benzoic acid) and an $\alpha 2\delta$ ligand (e.g. pregabalin), and pharmaceutically acceptable salts thereof, pharmaceutical compns. thereof and their use in the treatment of pain, particularly inflammatory, neuropathic, visceral and nociceptive pain. Although neither the compds. nor the methods of preparation are claimed, many example preps. (many of which are reproduced from previously published patents) are included. 4-[(1S)-1-[[[5-chloro-2-(3-fluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid and pregabalin were tested for effectiveness against carrageenan-induced mech. hyperalgesia and the combination was significantly more effective than either substance alone.

IC ICM A61K045-06

ICS A61K031-196; A61P025-02; A61P029-00

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1, 25, 27

IT 415902-95-3P, 2-Ethyl-5,7-dimethyl-3-[4-[2-[[[(4-methylphenyl)sulfonyl]amino]carbonyl]amino]ethyl]phenyl]-3H-imidazo[4,5-b]pyridine 415903-37-6P, 2-Ethyl-4,6-dimethyl-1-[4-[2-[[[(4-methylphenyl)sulfonyl]amino]carbonyl]amino]ethyl]phenyl]-1H-imidazo[4,5-c]pyridine **686766-31-4P**, (2S,4S)-4-(3-Fluorobenzyl)pyrrolidine-2-carboxylic acid monohydrochloride **686766-87-0P**, (2S,4S)-4-(3-Chlorophenoxy)pyrrolidine-2-carboxylic acid 847727-34-8P, 4-[[[[5-Fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-35-9P, 4-[1-[[[5-Fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 847727-36-0P, 4-[1-[[[5-Fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]propyl]benzoic acid 847727-37-1P, 4-[1-[[[5-Fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]-1-methylethyl]benzoic acid 847727-38-2P, 4-[(1S)-1-[[[5-Fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 847727-39-3P, 4-[(1S)-1-[[[5-Fluoro-2-(3-fluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 847727-40-6P, 4-[[[[5-Fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]-3-methylbenzoic acid 847727-41-7P, 3-Fluoro-4-[[[[5-fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-42-8P, 4-[[[[5-Fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]-2-methylbenzoic acid 847727-43-9P, 4-[[[[5-Fluoro-2-(3-methoxy-5-methylphenoxy)pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-44-0P, 4-[[[[2-(2-Chlorophenoxy)-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-45-1P, 4-[[[[2-(3-Chlorophenoxy)-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-46-2P, 4-[[[[2-[(2,3-Dihydro-1H-inden-5-yl)oxy]-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-47-3P, 4-[[[[2-(Biphenyl-4-yloxy)-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-48-4P, 4-[[[[2-(3-Chloro-4-methylphenoxy)-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-49-5P, 4-[[[[2-(3,5-Difluorophenoxy)-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-50-8P, 4-[[[[2-[(4-Cyclopentylphenyl)oxy]-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-51-9P, 4-[[[[5-Fluoro-2-(3-methoxyphenoxy)pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-52-0P, 4-[[[[5-Fluoro-2-phenoxy]pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-53-1P, 4-[[[[5-Fluoro-2-(2-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-54-2P, 4-[[[[2-[4-(Benzyloxy)phenoxy]-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-55-3P, 4-[[[[5-Fluoro-2-(3-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-56-4P, 4-[[[[2-[(3-Ethynylphenyl)oxy]-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-57-5P, 4-[[[[2-(2-Chloro-5-methylphenoxy)-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-58-6P, 4-[[[[2-(3-Chloro-4-fluorophenoxy)-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-59-7P, 4-[[[[2-(2,6-Difluorophenoxy)-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-60-0P, 4-[[[[2-[(3-Ethylphenyl)oxy]-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-61-1P, 4-[[[[2-(3,4-Difluorophenoxy)-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-62-2P, 4-[[[[5-Fluoro-2-[3-(trifluoromethoxy)phenoxy]pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-63-3P, 4-[[[[5-Fluoro-2-(4-fluoro-3-methylphenoxy)pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-64-4P, 4-[[[[2-(Biphenyl-3-yloxy)-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-65-5P, 4-[[[[5-Fluoro-2-[(3-methylphenyl)oxy]pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-66-6P, 4-[[[[2-(3-Acetylphenoxy)-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-67-7P, 4-[[[[5-Fluoro-2-(2-naphthyloxy)pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-68-8P, 4-[[[[5-Fluoro-2-(1-naphthyloxy)pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-69-9P, 4-[[[[2-[(4-Chloro-1-

naphthyl)oxy]-5-fluoropyridin-3-yl]carbonyl]amino]methyl]benzoic acid
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847727-72-4P, 4-[[[5-Fluoro-2-(quinolin-8-yloxy)pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-73-5P, 4-[[[5-Fluoro-2-[4-(2-methyl-1,3-thiazol-4-yl)phenoxy]pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-74-6P, 4-[[[5-Fluoro-2-[(5-fluoroquinolin-8-yl)oxy]pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-75-7P, 4-[[[5-Fluoro-2-[4-(pyridin-2-yl)phenyl]oxy]pyridin-3-yl]carbonyl]amino]methyl]benzoic acid 847727-76-8P, 4-[[[5-Chloro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]benzoic acid
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847727-81-5P, 4-[(1S)-1-[[[5-Chloro-2-(3-fluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 847727-82-6P, 4-[(1S)-1-[[[5-Chloro-2-(3-chlorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid
847727-83-7P, 4-[(1S)-1-[[[5-Chloro-2-(3-methoxyphenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 847727-84-8P, 4-[(1S)-1-[[[5-Chloro-2-(2,4-difluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid
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847728-09-0P, 5-Chloro-2-(4-fluorophenoxy)-N-[4-(2H-tetrazol-5-yl)benzyl]benzamide 847728-10-3P, 5-Chloro-2-(4-fluorophenoxy)-N-[(1S)-1-[4-(2H-tetrazol-5-yl)phenyl]ethyl]benzamide 847728-11-4P,

5-Fluoro-2-(4-fluorobenzyl)-N-[4-(2H-tetrazol-5-yl)benzyl]nicotinamide
847728-12-5P, 5-Chloro-N-[(1S)-1-[4-[[[(3-chlorophenyl)sulfonyl]amino]carbonyl]phenyl]ethyl]-2-(3-fluorophenoxy)nicotinamide 849487-80-5P,
(3R,4R,5R)-3-Amino-4,5-dimethyloctanoic acid 868561-89-1P
868635-72-7P, 4-[(1S)-1-[5-Chloro-2-[(2-chlorophenoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868635-76-1P, 4-[(1S)-1-[5-Chloro-2-[(3-chlorophenoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868635-80-7P,
4-[(1S)-1-[5-Chloro-2-[(4-chlorophenoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868635-84-1P, 4-[(1S)-1-[5-Chloro-2-[(4-fluorophenoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868635-88-5P,
4-[(1S)-1-[5-Chloro-2-[(3-fluorophenoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868635-92-1P, 4-[(1S)-1-[5-Chloro-2-[(2-fluorophenoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868635-96-5P,
4-[(1S)-1-[5-Chloro-2-[(2,3-difluorophenoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868636-00-4P, 4-[(1S)-1-[5-Chloro-2-[(2,4-difluorophenoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868636-07-1P,
4-[(1S)-1-[5-Chloro-2-[(2,5-difluorophenoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868636-14-0P, 4-[(1S)-1-[5-Chloro-2-[(2,6-difluorophenoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868636-19-5P,
4-[(1S)-1-[5-Chloro-2-[(3,4-difluorophenoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868636-23-1P, 4-[(1S)-1-[5-Chloro-2-[(3,5-difluorophenoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868636-27-5P,
4-[(1S)-1-[5-Chloro-2-[[4-methylphenyl]oxy]methyl]benzoyl]amino]ethyl]benzoic acid 868636-31-1P, 4-[(1S)-1-[5-Chloro-2-[(5-fluoropyridin-3-yl)oxy]methyl]benzoyl]amino]ethyl]benzoic acid 868636-35-5P,
4-[(1S)-1-[5-Chloro-2-[(5-chloropyridin-3-yl)oxy]methyl]benzoyl]amino]ethyl]benzoic acid 868636-39-9P, 4-[(1S)-1-[5-Chloro-2-[(cyclopentyloxy)methyl]benzoyl]amino]ethyl]benzoic acid 868636-42-4P,
4-[(1S)-1-[5-Chloro-2-(isobutoxymethyl)benzoyl]amino]ethyl]benzoic acid 868636-45-7P, 4-[(1S)-1-[5-Chloro-2-[(4-chlorophenoxy)methyl]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868636-49-1P, 4-[(1S)-1-[5-Chloro-2-[[3-[(methylamino)carbonyl]phenoxy]methyl]benzoyl]amino]ethyl]benzoic acid 868636-53-7P, 4-[(1S)-1-[5-Chloro-2-[(3-chlorophenoxy)methyl]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868636-56-0P, 4-[(1S)-1-[2-[(4-chlorophenoxy)methyl]-5-fluoropyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868636-62-8P, 4-[(1S)-1-[5-Chloro-2-[(5-chloropyridin-2-yl)(methyl)amino]methyl]benzoyl]amino]ethyl]benzoic acid 868636-66-2P, 4-[(1S)-1-[5-Chloro-2-[(cyclohexylmethoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868636-69-5P, 4-[(1S)-1-[5-Chloro-2-[(2,2-dimethylpropoxy)methyl]benzoyl]amino]ethyl]benzoic acid 868636-71-9P, 4-[(1S)-1-[5-Chloro-2-[(5-fluoropyridin-2-yl)(methyl)amino]methyl]benzoyl]amino]ethyl]benzoic acid 868636-75-3P, 4-[(1S)-1-[5-Chloro-2-[(3-fluorophenoxy)methyl]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868636-82-2P, 4-[(1S)-1-[5-Chloro-2-[(4-fluorophenoxy)methyl]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868636-86-6P, 4-[[5-Chloro-2-(2-phenylethoxy)benzoyl]amino]methyl]benzoic acid 868636-87-7P, 4-[[5-Chloro-2-[2-(2-chlorophenyl)ethoxy]benzoyl]amino]methyl]benzoic acid 868636-88-8P, 4-[[5-Chloro-2-[2-(4-fluorophenyl)ethoxy]benzoyl]amino]methyl]benzoic acid 868636-89-9P, 4-[[5-Chloro-2-[2-(4-chlorophenyl)ethoxy]benzoyl]amino]methyl]benzoic acid 868636-90-2P, 4-[[5-Chloro-2-(cyclohexyloxy)benzoyl]amino]methyl]benzoic acid 868636-91-3P, 4-[[5-Chloro-2-[(4-chlorobenzyl)oxy]benzoyl]amino]methyl]benzoic acid 868636-92-4P, 4-[[5-Chloro-2-[2-(2-methylphenyl)ethoxy]benzoyl]amino]methyl]benzoic acid 868636-94-6P, 4-[(1S)-1-[5-Chloro-2-[2-(2,6-difluorophenyl)ethoxy]benzoyl]amino]ethyl]benzoic acid 868636-97-9P, 4-[(1S)-1-[5-Chloro-2-[2-(4-fluorophenyl)ethoxy]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868637-00-7P, 4-[(1S)-1-[5-Chloro-2-[2-(2-fluorophenyl)ethoxy]benzoyl]amino]ethyl]benzoic acid 868637-02-9P, 4-[(1S)-1-[5-Chloro-2-[2-(2-methylphenyl)ethoxy]benzoyl]amino]ethyl]benzoic acid 868637-04-1P,

4-[(1S)-1-[[5-Chloro-2-[2-(4-methylphenyl)ethoxy]benzoyl]amino]ethyl]benzoic acid 868637-06-3P, 4-[(1S)-1-[[5-Chloro-2-(cyclohexyloxy)benzoyl]amino]ethyl]benzoic acid 868637-08-5P, 4-[(1S)-1-[[5-Chloro-2-(3-methylbutoxy)benzoyl]amino]ethyl]benzoic acid 868637-10-9P, 4-[(1S)-1-[[[5-Chloro-2-[2-(4-chlorophenyl)ethoxy]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868637-13-2P, 4-[(1S)-1-[[[5-Chloro-2-[methyl(2-phenylethyl)amino]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868637-15-4P, 4-[(1S)-1-[[5-Chloro-2-[(cis-4-methylcyclohexyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-18-7P, 4-[(1S)-1-[[5-Chloro-2-[(trans-4-methylcyclohexyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-19-8P, 4-[(1S)-1-[[[5-Chloro-2-[2-(2-methylphenyl)ethoxy]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868637-22-3P, 4-[(1S)-1-[[5-Chloro-2-(3-methoxy-3-methylbutoxy)benzoyl]amino]ethyl]benzoic acid 868637-24-5P, 4-[(1S)-1-[[5-Chloro-2-(2-isopropoxyethoxy)benzoyl]amino]ethyl]benzoic acid 868637-26-7P, 4-[(1S)-1-[[5-Chloro-2-[(2-chlorobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-28-9P, 4-[(1S)-1-[[5-Chloro-2-[(3-chlorobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-30-3P, 4-[(1S)-1-[[5-Chloro-2-[(4-chlorobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-32-5P, 4-[(1S)-1-[[5-Chloro-2-[(4-fluorobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-34-7P, 4-[(1S)-1-[[5-Chloro-2-(2-phenoxyethoxy)benzoyl]amino]ethyl]benzoic acid 868637-36-9P, 4-[(1S)-1-[[5-Chloro-2-(2-methoxy-2-phenylethoxy)benzoyl]amino]ethyl]benzoic acid 868637-38-1P, 4-[(1S)-1-[[5-Chloro-2-[2-(4-fluorophenoxy)ethoxy]benzoyl]amino]ethyl]benzoic acid 868637-40-5P, 4-[(1S)-1-[[5-Chloro-2-(cyclobutylmethoxy)benzoyl]amino]ethyl]benzoic acid 868637-42-7P, 4-[(1S)-1-[[5-Chloro-2-isobutoxybenzoyl]amino]ethyl]benzoic acid 868637-44-9P, 4-[(1S)-1-[[[5-Chloro-2-(3-methylbutoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868637-47-2P, 4-[(1S)-1-[[5-Chloro-2-[(2,5-difluorobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-49-4P, 4-[(1S)-1-[[5-Chloro-2-[(3,4-difluorobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-51-8P, 4-[(1S)-1-[[5-Chloro-2-[2-(4-fluorophenyl)ethoxy]benzoyl]amino]ethyl]benzoic acid 868637-53-0P, 4-[(1S)-1-[[5-Chloro-2-[(2,4-difluorobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-55-2P, 4-[(1S)-1-[[5-Chloro-2-[(2-fluorobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-57-4P, 4-[(1S)-1-[[5-Chloro-2-[(3,5-difluorobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-60-9P, 4-[(1S)-1-[[[5-Chloro-2-[(2-chlorobenzyl)oxy]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868637-63-2P, 4-[(1S)-1-[[[5-Chloro-2-[(4-chlorobenzyl)oxy]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868637-66-5P, 4-[(1S)-1-[[5-Chloro-2-[(2-cyanobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-68-7P, 4-[(1S)-1-[[5-Chloro-2-[2-(tetrahydro-2H-pyran-4-yl)ethoxy]benzoyl]amino]ethyl]benzoic acid 868637-70-1P, 4-[(1S)-1-[[5-Chloro-2-[(3-fluorobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-72-3P, 4-[(1S)-1-[[5-Chloro-2-[(5-methylisoxazol-3-yl)methoxy]benzoyl]amino]ethyl]benzoic acid 868637-74-5P, 4-[(1S)-1-[[5-Chloro-2-[(4-chloro-2-fluorobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-76-7P, 4-[(1S)-1-[[5-Chloro-2-[(2-chloro-4-fluorobenzyl)oxy]benzoyl]amino]ethyl]benzoic acid 868637-78-9P, 4-[(1S)-1-[[5-Chloro-2-[(3-chloropyridin-2-yl)methoxy]benzoyl]amino]ethyl]benzoic acid 868637-80-3P, 4-[(1S)-1-[[[5-Chloro-2-[(2-chlorobenzyl)(methyl)amino]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868637-82-5P, 4-[(1S)-1-[[5-Chloro-2-(tetrahydrofuran-2-yl)methoxy]benzoyl]amino]ethyl]benzoic acid 868637-84-7P, 4-[(1S)-1-[[[5-Chloro-2-[(2-fluorobenzyl)(methyl)amino]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868637-85-8P, 4-[(1S)-1-[[[5-Chloro-2-[(4-chlorobenzyl)(methyl)amino]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868637-88-1P, 4-[(1S)-1-[[[5-Chloro-2-[(3-

chlorobenzyl) (methyl) amino]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid
 868637-90-5P, 4-[(1S)-1-[[[5-Chloro-2-[(3-fluorobenzyl) (methyl) amino]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid 868637-92-7P,
 4-[(1S)-1-[[[5-Chloro-2-[(4-fluorobenzyl) (methyl) amino]pyridin-3-yl]carbonyl]amino]ethyl]benzoic acid

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(codrug; combinations comprising EP4-receptor antagonists and $\alpha 2\delta$ ligands for treating pain)

IT 60142-96-3, Gabapentin 148553-50-8, Pregabalin 223445-75-8,
 ((3S,4S)-1-Aminomethyl-3,4-dimethylcyclopentyl)acetic acid 227625-35-6,
 3-[(1-Aminomethylcyclohexyl)methyl]-4H-[1,2,4]oxadiazol-5-one
 227626-51-9, [[1-(1H-Tetrazol-5-ylmethyl)cycloheptyl]methyl]amine
 313651-33-1, (3S,5R)-3-Aminomethyl-5-methyloctanoic acid 335458-65-6,
 [(1 α ,3 α ,5 α)-3-Aminomethylbicyclo[3.2.0]hept-3-yl]acetic
 acid 415904-13-1, 4-(6-Chloro-2-ethyl-5-trifluoromethyl-1H-benzimidazol-1-yl)phenethyl [(4-methylphenyl)sulfonyl]carbamate 415906-01-3,
 2-[4-[2-(1,1-Dimethylethyl)-4,6-dimethyl-1H-imidazo[4,5-c]pyridin-1-yl]phenyl]ethyl [(4-methylphenyl)sulfonyl]carbamate 415906-55-7,
 2-[4-[6-Chloro-2-ethyl-5-(trifluoromethyl)-1H-benzimidazol-1-yl]phenyl]ethyl [(5-methyl-2-pyridinyl)sulfonyl]carbamate 415906-57-9,
 2-[5-[6-Chloro-2-ethyl-5-(trifluoromethyl)-1H-benzimidazol-1-yl]-2-pyridinyl]ethyl [(4-methylphenyl)sulfonyl]carbamate 415906-73-9,
 N-[[[2-[4-[5,7-Dimethyl-2-(methylamino)-3H-imidazo[4,5-b]pyridin-3-yl]phenyl]ethyl]amino]carbonyl]-4-methylbenzenesulfonamide 415906-78-4,
 2-[4-[5,7-Dimethyl-2-(methylamino)-3H-imidazo[4,5-b]pyridin-3-yl]phenyl]ethyl [(4-methylphenyl)sulfonyl]carbamate 415906-83-1,
 2-[4-[6-Chloro-2-(4-pyridinyl)-5-(trifluoromethyl)-1H-benzimidazol-1-yl]phenyl]ethyl [(4-methylphenyl)sulfonyl]carbamate 415907-18-5,
 N-[[[2-[4-[2-Ethyl-5-(1-hydroxy-1-methylethyl)-1H-benzimidazol-1-yl]phenyl]ethyl]amino]carbonyl]-4-methylbenzenesulfonamide 415907-55-0,
 6-Chloro-2-ethyl-1-[4-[2-[N-methyl[[[(4-methylphenyl)sulfonyl]amino]carbon yl]amino]ethyl]phenyl]-1H-benzimidazole-5-carboxamide 416844-64-9,
 5-Acetyl-2-ethyl-3-[4-[2-[[[(4-methylphenyl)sulfonyl]amino]carbonyl]amino]ethyl]phenyl]benzimidazole 473924-33-3, [(1R,5R,6S)-6-(Aminomethyl)bicyclo[3.2.0]hept-6-yl]acetic acid 610300-07-7,
 (3S,5R)-3-Amino-5-methyloctanoic acid 610300-19-1, (3S,5R)-3-Amino-5-methylheptanoic acid 610300-20-4, (3S,5R)-3-Amino-5-methylnonanoic acid 616877-19-1, 2-[4-(3,5-Dimethyl-4-phenyl-1H-pyrazol-1-yl)phenyl]ethyl [(4-methylphenyl)sulfonyl]carbamate 616877-21-5, 2-[4-[4-(4-Fluorophenyl)-3,5-dimethyl-1H-pyrazol-1-yl]phenyl]ethyl [(4-methylphenyl)sulfonyl]carbamate 616877-23-7, N-[[[2-[4-(3,5-Dimethyl-4-phenyl-1H-pyrazol-1-yl)phenyl]ethyl]amino]carbonyl]-4-methylbenzenesulfonamide 616877-24-8, N-[[[2-[4-[4-(4-Ethoxyphenyl)-3,5-dimethyl-1H-pyrazol-1-yl]phenyl]ethyl]amino]carbonyl]-4-methylbenzenesulfonamide 616877-26-0, N-[[[2-[4-(3,5-Dimethyl-4-phenyl-1H-pyrazol-1-yl)phenyl]ethyl]amino]carbonyl]-4-methoxybenzenesulfonamide 616877-31-7, N-[[[2-[4-(3,5-Dimethyl-4-phenyl-1H-pyrazol-1-yl)phenyl]ethyl]amino]carbonyl]-2-fluorobenzenesulfonamide 616877-32-8, N-[[[2-[4-(3,5-Dimethyl-4-phenyl-1H-pyrazol-1-yl)phenyl]ethyl]amino]carbonyl]-3,4-dimethoxybenzenesulfonamide 616877-33-9, N-[[[2-[4-(3,5-Dimethyl-4-phenyl-1H-pyrazol-1-yl)phenyl]ethyl]amino]carbonyl]-2,4-difluorobenzenesulfonamide 616877-35-1, 2,4-Difluoro-N-[[[2-[4-[5-methyl-4-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]ethyl]amino]carbonyl]benzenesulfonamide 616877-36-2, 2-Fluoro-N-[[[2-[4-[5-methyl-4-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]ethyl]amino]carbonyl]benzenesulfonamide 616892-63-8, 2-[4-(2-Amino-4,5-diphenyl-1H-imidazol-1-yl)phenyl]ethyl [(4-methylphenyl)sulfonyl]carbamate 616892-65-0, 2-[4-(2-Ethyl-4-phenyl-

1H-imidazol-1-yl)phenyl]ethyl [(4-methylphenyl)sulfonyl]carbamate
 616892-67-2, N-[[[2-[4-(2-Ethyl-4-phenyl-1H-imidazol-1-yl)phenyl]ethyl]amino]carbonyl]-4-methylbenzenesulfonamide 616892-69-4,
 2-Chloro-N-[[[2-[4-(2-ethyl-4-phenyl-1H-imidazol-1-yl)phenyl]ethyl]amino]carbonyl]benzenesulfonamide 616892-73-0,
 2-[4-(2-Butyl-4-phenyl-1H-imidazol-1-yl)phenyl]ethyl [(2-chlorophenyl)sulfonyl]carbamate 616892-75-2, 2-[4-(2-Isobutyl-4-phenyl-1H-imidazol-1-yl)phenyl]ethyl [(2-chlorophenyl)sulfonyl]carbamate 616892-77-4, 2-[4-(2-Isopropyl-4-phenyl-1H-imidazol-1-yl)phenyl]ethyl [(2-chlorophenyl)sulfonyl]carbamate 616892-79-6, 4-Chloro-N-[[[2-[4-(2-ethyl-4-phenyl-1H-imidazol-1-yl)phenyl]ethyl]amino]carbonyl]benzenesulfonamide 616892-81-0, 2-[4-(2-tert-Butyl-4-phenyl-1H-imidazol-1-yl)phenyl]ethyl [(2-chlorophenyl)sulfonyl]carbamate 616892-82-1,
 4-Chloro-N-[[[2-[4-(2-isopropyl-4-phenyl-1H-imidazol-1-yl)phenyl]ethyl]amino]carbonyl]benzenesulfonamide **688007-58-1**
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(codrug; combinations comprising EP4-receptor antagonists and $\alpha\delta$ ligands for treating pain)

IT 78-83-1, 2-Methylpropan-1-ol, reactions 79-03-8, Propionyl chloride 94-64-4, (2-Chlorobenzyl)methylamine 95-57-8, 2-Chlorophenol 96-41-3, Cyclopentanol 97-99-4, Tetrahydrofuran-2-ylmethanol 100-39-0, Benzyl bromide 100-49-2, Cyclohexylmethanol 104-10-9, 2-(4-Aminophenyl)ethyl alcohol 104-11-0, (4-Chlorobenzyl)methylamine 106-44-5, 4-Methylphenol, reactions 106-48-9, 4-Chlorophenol 108-43-0, 3-Chlorophenol 108-93-0, Cyclohexanol, reactions 109-59-1, 2-Isopropoxyethanol 122-99-6, 2-Phenoxyethanol 123-51-3, 3-Methylbutan-1-ol 123-54-6, 2,4-Pentanedione, reactions 123-62-6, Propionic anhydride 141-78-6, Ethyl acetate, reactions 150-19-6, 3-Methoxyphenol 321-14-2, 5-Chloro-2-hydroxybenzoic acid 348-60-7, 4-Chloro-3-fluorophenol 367-12-4, 2-Fluorophenol 367-27-1, 2,4-Difluorophenol 371-41-5, 4-Fluorophenol 372-20-3, 3-Fluorophenol 399-30-4, (2-Fluorobenzyl)methylamine 405-66-3, (4-Fluorobenzyl)methylamine 446-48-0, 1-(Bromomethyl)-2-fluorobenzene 456-41-7, 1-(Bromomethyl)-3-fluorobenzene 459-56-3, (4-Fluorophenyl)methanol 501-53-1, Benzyl chloroformate 589-08-2, (2-Phenylethyl)methylamine 589-91-3, 4-Methylcyclohexanol 699-02-5, 2-(4-Methylphenyl)ethanol 873-62-1, 3-Hydroxybenzonitrile 873-63-2, (3-Chlorophenyl)methanol 873-76-7, (4-Chlorophenyl)methanol 1875-88-3, 2-(4-Chlorophenyl)ethanol 1996-41-4, 2-Chloro-4-fluorophenol 2252-51-9, 2-Chloro-4-fluorobenzoic acid 2713-31-7, 2,5-Difluorophenol 2713-33-9, 3,4-Difluorophenol 2713-34-0, 3,5-Difluorophenol 2924-66-5, 2-(4-Fluorophenoxy)ethanol 2979-22-8, 2-Methoxy-2-phenylethanol 4083-64-1, p-Toluenesulfonyl isocyanate 4214-80-6, 5-Chloro-N-methylpyridin-2-amine 4415-82-1, Cyclobutylmethanol 4677-18-3, 2-(Tetrahydro-2H-pyran-4-yl)ethanol 6148-64-7, Potassium ethyl malonate 6232-11-7, Methyl 4-(aminomethyl)benzoate hydrochloride 6418-38-8, 2,3-Difluorophenol 7589-27-7, 2-(4-Fluorophenyl)ethanol 15513-48-1, 4-Chloro-2,6-dimethyl-3-nitropyridine 15788-97-3, 3-Hydroxy-N-methylbenzamide 16957-70-3, (E)-2-Methyl-2-pentenoic acid 17260-71-8, 3-Chlorobenzenesulfonamide 17849-38-6, (2-Chlorophenyl)methanol 19819-98-8, 2-(2-Methylphenyl)ethanol 21717-96-4, 5-Fluoropyridin-2-amine 22115-41-9, 2-(Bromomethyl)benzonitrile 23190-16-1, (1R,2S)-Diphenyl-2-aminoethanol 23915-07-3, 1-(Bromomethyl)-2,4-difluorobenzene 24358-62-1, [1-(4-Bromophenyl)ethyl]amine 27298-97-1, [(1S)-1-(4-Bromophenyl)ethyl]amine 28177-48-2, 2,6-Difluorophenol 35166-37-1, 3-(Chloromethyl)-5-methylisoxazole 35582-13-9, 3-(1,3-Thiazol-2-yl)phenol 38186-88-8, 2-Chloro-5-fluoronicotinic acid 39191-07-6, (3-Chlorobenzyl)methylamine 50919-06-7, 2-(2-Fluorophenyl)ethanol 56456-49-6, (4-Chloro-2-fluorophenyl)methanol

56539-66-3, 3-Methoxy-3-methylbutan-1-ol 57381-36-9, Methyl
 5-chloro-2-fluorobenzoate 59782-85-3, 2,5-Dichloronicotinic acid
 60588-81-0, (3-Chloropyridin-2-yl)methanol 67754-03-4, Methyl
 2,5-dichloronicotinate 74115-12-1, 3-Chloro-5-hydroxypyridine
 74844-91-0, (2S,4R)-4-Hydroxypyrrolidine-1,2-dicarboxylic acid
 1-tert-butyl ester 2-methyl ester 78686-79-0, Methyl
 5-bromo-2-chloronicotinate 78686-83-6, Methyl 2-chloro-5-iodonicotinate
 79361-96-9, Methyl 4-(1-amino-1-methylethyl)benzoate 85117-99-3,
 2-(Bromomethyl)-1,4-difluorobenzene 85118-01-0, 4-(Bromomethyl)-1,2-
 difluorobenzene 90389-84-7, (3-Fluorobenzyl)methylamine 97961-66-5,
 (E)-2-Methyl-2-hexenoic acid 99395-88-7, (S)-(+)-4-Phenyloxazolidin-2-
 one 104961-03-7, 5-Fluoro-2-(4-fluorophenoxy)benzoic acid 107045-28-3,
 tert-Butyl 4-(aminomethyl)benzoate 117269-72-4, (3-Cyanobenzyl)zinc
 bromide 141776-91-2, 1-(Bromomethyl)-3,5-difluorobenzene 168766-16-3,
 2-(2,6-Difluorophenyl)ethanol 177595-28-7, 1-[4-(2H-Tetrazol-5-
 yl)phenyl]methanamine monohydrochloride 208186-84-9,
 (2-Chloro-4-fluorophenyl)methanol 209328-55-2, 3-Fluoro-5-
 hydroxypyridine 222714-33-2, 4-((1S)-1-Aminoethyl)benzoic acid
 225528-27-8, Methyl 4-(aminomethyl)-3-fluorobenzoate 229954-45-4,
 4-Cyanobenzylhexamine hydrobromide 312624-13-8, (3-Chlorobenzyl)zinc
 chloride 312693-06-4, (3-Fluorobenzyl)zinc chloride 312693-07-5,
 (4-Fluorobenzyl)zinc chloride 312693-16-6, (3-Methoxybenzyl)zinc
 chloride 325855-78-5, Methyl 5-chloro-2-methylnicotinate 1-oxide
 444807-72-1, 5-Chloro-2-(4-fluorophenoxy)nicotinic acid 503470-24-4,
 Methyl 4-(aminomethyl)-2-methylbenzoate 503470-27-7, Methyl
 4-(aminomethyl)-3-methylbenzoate 668262-52-0, Methyl
 2-(bromomethyl)-5-chlorobenzoate **686766-69-8** 847730-67-0,
 Methyl 4-(1-aminopropyl)benzoate 847730-68-1, Methyl
 4-(aminomethyl)-2-fluorobenzoate

RL: RCT (Reactant); RACT (Reactant or reagent)

(combinations comprising EP4-receptor antagonists and $\alpha 2\delta$
 ligands for treating pain)

IT 22934-13-0P, 4,6-Dimethyl-3-nitro-2(1H)-pyridinone 23204-70-8P,
 (4S,5R)-4,5-Diphenyloxazolidin-2-one 69199-64-0P, 5-Chloro-2-(3-
 chlorophenoxy)benzoic acid 69199-73-1P, 5-Chloro-2-(3-
 methoxyphenoxy)benzoic acid 89793-09-9P, 2-Chloro-4,6-dimethyl-3-
 nitropyridine 108476-28-4P, Methyl 5-chloro-2-(3-chlorophenoxy)benzoate
 148065-10-5P, Ethyl 2,5-dichloronicotinate 415907-57-2P,
 2-[4-[(4,6-Dimethyl-3-nitro-2-pyridinyl)amino]phenyl]ethanol 415907-58-3
 P, 2-[4-[(3-Amino-4,6-dimethyl-2-pyridinyl)amino]phenyl]ethanol
 415907-59-4P, 2-[4-(2-Ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-
 yl)phenyl]ethyl propionate 415907-60-7P, 2-[4-(2-Ethyl-5,7-dimethyl-3H-
 imidazo[4,5-b]pyridin-3-yl)phenyl]ethanol 415907-61-8P,
 3-[4-(2-Chloroethyl)phenyl]-2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridine
 415907-62-9P, 2-[4-(2-Ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-
 yl)phenyl]ethyl azide 415907-63-0P, [2-[4-(2-Ethyl-5,7-dimethyl-3H-
 imidazo[4,5-b]pyridin-3-yl)phenyl]ethyl]amine 415908-90-6P,
 2-[4-[(2,6-Dimethyl-3-nitro-4-pyridinyl)amino]phenyl]ethanol
 415908-91-7P, 2-[4-[(3-Amino-2,6-dimethyl-4-pyridinyl)amino]phenyl]ethanol
 415908-92-8P, 2-[4-(2-Ethyl-4,6-dimethyl-1H-imidazo[4,5-c]pyridin-1-
 yl)phenyl]ethyl propionate 415908-93-9P, 2-[4-(2-Ethyl-4,6-dimethyl-1H-
 imidazo[4,5-c]pyridin-1-yl)phenyl]ethanol 415908-94-0P,
 1-[4-(2-Chloroethyl)phenyl]-2-ethyl-4,6-dimethyl-1H-imidazo[4,5-c]pyridine
 415908-95-1P, 1-[4-(2-Azidoethyl)phenyl]-2-ethyl-4,6-dimethyl-1H-
 imidazo[4,5-c]pyridine 415908-96-2P, [2-[4-(2-Ethyl-4,6-dimethyl-1H-
 imidazo[4,5-c]pyridin-1-yl)phenyl]ethyl]amine **686766-55-2P**,
 (2S,4S)-4-(3-Chlorophenoxy)pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl
 ester 2-methyl ester **686766-56-3P** **686766-74-5P**
 847728-82-9P 847728-83-0P, 5-Fluoro-2-(4-fluorophenoxy)nicotinic acid
 847728-84-1P, Methyl 4-[[[5-fluoro-2-(4-fluorophenoxy)pyridin-3-

yl]carbonyl]amino]methyl]benzoate 847728-85-2P, N-[1-(4-Bromophenyl)ethyl]-5-fluoro-2-(4-fluorophenoxy)nicotinamide
 847728-86-3P, Methyl 4-[1-[[[5-fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847728-87-4P, Methyl
 4-[1-[[[5-fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]propyl]benzoate 847728-88-5P, Methyl
 4-[1-[[[5-fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]-1-methylethyl]benzoate 847728-89-6P, tert-Butyl [(1S)-1-(4-bromophenyl)ethyl]carbamate 847728-90-9P, Methyl 4-[(1S)-1-[(tert-butoxycarbonyl)amino]ethyl]benzoate 847728-91-0P, Methyl
 4-[(1S)-1-aminoethyl]benzoate hydrochloride 847728-92-1P, Methyl
 4-[(1S)-1-[[[5-fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847728-93-2P, 5-Fluoro-2-(3-fluorophenoxy)nicotinic acid 847728-94-3P, Methyl 4-[(1S)-1-[[[5-fluoro-2-(3-fluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate
 847728-95-4P, Methyl 4-[[[5-fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]-3-methylbenzoate 847728-96-5P, Methyl
 3-fluoro-4-[[[5-fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]benzoate 847728-97-6P, Methyl
 4-[[[5-fluoro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]-2-methylbenzoate 847728-98-7P, tert-Butyl 4-[[[(2-chloro-5-fluoropyridin-3-yl)carbonyl]amino]methyl]benzoate 847728-99-8P, Methyl
 4-[[[5-chloro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]benzoate 847729-00-4P, 4-[(1S)-1-[(Benzoyloxy)carbonyl]amino]ethyl]benzoic acid 847729-01-5P, tert-Butyl 4-[(1S)-1-[(benzyloxy)carbonyl]amino]ethyl]benzoate 847729-02-6P, tert-Butyl 4-[(1S)-1-aminoethyl]benzoate
 847729-03-7P, tert-Butyl 4-[(1S)-1-[[[5-Chloro-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-04-8P, tert-Butyl
 4-[(1S)-1-[[[2,5-dichloropyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-05-9P, tert-Butyl 4-[(1S)-1-[[[5-chloro-2-[3-(1,3-thiazol-2-yl)phenoxy]pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-06-0P,
 5-Chloro-2-[(5-chloropyridin-3-yl)oxy]nicotinic acid 847729-07-1P, tert-Butyl 4-[(1S)-1-[[[5-chloro-2-[(5-chloropyridin-3-yl)oxy]pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-08-2P, 5-Chloro-2-(3-cyanophenoxy)nicotinic acid 847729-09-3P, tert-Butyl
 4-[(1S)-1-[[[5-chloro-2-(3-cyanophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-10-6P, Methyl
 4-[(1S)-1-[[[2,5-dichloropyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-13-9P, tert-Butyl 4-[(1S)-1-[[[5-chloro-2-(3-methoxyphenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-15-1P, tert-Butyl
 4-[(1S)-1-[[[5-chloro-2-(4-chloro-3-fluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-18-4P, tert-Butyl
 4-[(1S)-1-[[[5-chloro-2-(3,4-difluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-19-5P, Methyl
 2-(4-fluorophenoxy)-5-iodonicotinate 847729-20-8P 847729-21-9P,
 2-(4-Fluorophenoxy)-5-(trifluoromethyl)nicotinic acid 847729-22-0P,
 Methyl 4-[[[2-(4-fluorophenoxy)-5-(trifluoromethyl)pyridin-3-yl]carbonyl]amino]methyl]benzoate 847729-23-1P, Methyl
 5-bromo-2-(4-fluorophenoxy)nicotinate 847729-24-2P, Methyl
 5-cyano-2-(4-fluorophenoxy)nicotinate 847729-25-3P, 5-Cyano-2-(4-fluorophenoxy)nicotinic acid 847729-26-4P, Methyl 4-[[[5-cyano-2-(4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]methyl]benzoate 847729-27-5P,
 Methyl 2-chloro-5-fluoronicotinate 847729-28-6P, Methyl
 5-fluoro-2-(4-fluorobenzyl)nicotinate 847729-29-7P, 5-Fluoro-2-(4-fluorobenzyl)nicotinic acid 847729-30-0P, Methyl 4-[[[5-fluoro-2-(4-fluorobenzyl)pyridin-3-yl]carbonyl]amino]methyl]benzoate 847729-31-1P,
 Methyl 4-[(1S)-1-[[[5-fluoro-2-(4-fluorobenzyl)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-32-2P, Methyl
 5-chloro-2-(4-fluorobenzyl)nicotinate 847729-33-3P, 5-Chloro-2-(4-fluorobenzyl)nicotinic acid 847729-34-4P, Methyl 4-[(1S)-1-[[[5-chloro-2-

(4-fluorobenzyl)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-35-5P,
Methyl 5-chloro-2-(3-fluorobenzyl)nicotinate 847729-36-6P,
5-Chloro-2-(3-fluorobenzyl)nicotinic acid 847729-37-7P, Methyl
4-[(1S)-1-[[[5-chloro-2-(3-fluorobenzyl)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-38-8P, Methyl
5-chloro-2-(3-chlorobenzyl)nicotinate 847729-39-9P, 5-Chloro-2-(3-chlorobenzyl)nicotinic acid 847729-40-2P, Methyl 4-[(1S)-1-[[[5-chloro-2-(3-chlorobenzyl)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-41-3P,
Methyl 5-chloro-2-(3-methoxybenzyl)nicotinate 847729-42-4P,
5-Chloro-2-(3-methoxybenzyl)nicotinic acid 847729-43-5P, Methyl
4-[(1S)-1-[[[5-chloro-2-(3-methoxybenzyl)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-44-6P, Methyl
5-chloro-2-(3-cyanobenzyl)nicotinate 847729-45-7P, 5-Chloro-2-(3-cyanobenzyl)nicotinic acid 847729-46-8P, Methyl 4-[(1S)-1-[[[5-chloro-2-(3-cyanobenzyl)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 847729-47-9P,
Methyl 4-[[[5-fluoro-2-(4-fluorophenoxy)benzoyl]amino]methyl]benzoate 847729-48-0P, 4-Fluoro-2-(4-fluorophenoxy)benzoic acid 847729-49-1P,
Methyl 4-[[[4-fluoro-2-(4-fluorophenoxy)benzoyl]amino]methyl]benzoate 847729-50-4P, Methyl 5-chloro-2-(4-fluorophenoxy)benzoate 847729-51-5P,
5-Chloro-2-(4-fluorophenoxy)benzoic acid 847729-52-6P, Methyl
4-[[[5-chloro-2-(4-fluorophenoxy)benzoyl]amino]methyl]benzoate 847729-53-7P, Methyl 4-[(1S)-1-[[[5-chloro-2-(4-fluorophenoxy)benzoyl]amino]ethyl]benzoate 847729-54-8P, Methyl
4-[[[5-chloro-2-(4-fluorophenoxy)benzoyl]amino]methyl]-2-fluorobenzoate 847729-55-9P, Methyl 4-[(1S)-1-[[[5-chloro-2-(3-chlorophenoxy)benzoyl]amino]ethyl]benzoate 847729-56-0P, Methyl
5-chloro-2-(3-fluorophenoxy)benzoate 847729-57-1P, 5-Chloro-2-(3-fluorophenoxy)benzoic acid 847729-58-2P, Methyl 4-[(1S)-1-[[[5-chloro-2-(3-fluorophenoxy)benzoyl]amino]ethyl]benzoate 847729-59-3P, Methyl
5-chloro-2-(3-methoxyphenoxy)benzoate 847729-60-6P, Methyl
4-[(1S)-1-[[[5-chloro-2-(3-methoxyphenoxy)benzoyl]amino]ethyl]benzoate 847729-61-7P, N-(4-Cyanobenzyl)-5-fluoro-2-(4-fluorophenoxy)nicotinamide 847729-62-8P,
5-Chloro-N-(4-cyanobenzyl)-2-(4-fluorophenoxy)nicotinamide 847729-63-9P, tert-Butyl [(1S)-1-(4-cyanophenyl)ethyl]carbamate 847729-64-0P, tert-Butyl [(1S)-1-[4-(2H-tetrazol-5-yl)phenyl]ethyl]carbamate 847729-65-1P, [(1S)-1-[4-(2H-Tetrazol-5-yl)phenyl]ethyl]amine monohydrochloride 866108-40-9P,
(S)-3-((E)-2-Methylpent-2-enoyl)-4-phenyloxazolidin-2-one 866108-41-0P,
(4S,5R)-3-((E)-2-Methylpent-2-enoyl)-4,5-diphenyloxazolidin-2-one 866108-42-1P, (4S)-3-((2R,3R)-2,3-Dimethylpentanoyl)-4-phenyloxazolidin-2-one 866108-43-2P, (4R,5R)-4,5-Dimethyl-3-oxoheptanoic acid ethyl ester 866108-44-3P, (4R,5R)-3-(Methoxyimino)-4,5-dimethylheptanoic acid ethyl ester 866108-46-5P, (4R,5R,2Z)-3-Amino-4,5-dimethylhept-2-enoic acid ethyl ester 866108-47-6P, (4R,5R,2Z)-3-Acetylamino-4,5-dimethylhept-2-enoic acid ethyl ester 866108-49-8P, (3R,4R,5R)-3-Acetylamino-4,5-dimethylheptanoic acid ethyl ester 866108-52-3P 866108-55-6P,
(4S,5R)-3-((2R,3R)-2,3-Dimethylhexanoyl)-4,5-diphenyloxazolidin-2-one 866108-59-0P, (4R,5R)-4,5-Dimethyl-3-oxooctanoic acid ethyl ester 866108-60-3P, (2R,3R)-2,3-Dimethylhexanoyl chloride 866108-62-5P,
(4R,5R)-3-(Methoxyamino)-4,5-dimethyl-(Z)-oct-2-enoic acid ethyl ester 866108-64-7P, (4R,5R)-3-Amino-4,5-dimethyl-(Z)-oct-2-enoic acid ethyl ester 866108-66-9P, (4R,5R,2Z)-3-Acetylamino-4,5-dimethyloct-2-enoic acid ethyl ester 866108-68-1P, (3R,4R,5R)-3-Acetylamino-4,5-dimethyloctanoic acid ethyl ester 868635-67-0P, tert-Butyl
4-[(1S)-1-[[[5-chloro-2-(3-fluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 868635-68-1P, tert-Butyl
4-[(1S)-1-[[[5-chloro-2-(3-chlorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 868635-69-2P, tert-Butyl
4-[(1S)-1-[[[5-chloro-2-(2,4-difluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 868635-70-5P, tert-Butyl

4-[(1S)-1-[[[5-chloro-2-(2-chloro-4-fluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 868635-71-6P, tert-Butyl
4-[(1S)-1-[[[5-chloro-2-(2,6-difluorophenoxy)pyridin-3-yl]carbonyl]amino]ethyl]benzoate 868635-73-8P, Methyl
5-chloro-2-[(2-chlorophenoxy)methyl]benzoate 868635-74-9P,
5-Chloro-2-[(2-chlorophenoxy)methyl]benzoic acid 868635-75-0P, Methyl
4-[(1S)-1-[[[5-chloro-2-[(2-chlorophenoxy)methyl]benzoyl]amino]ethyl]benzoate 868635-77-2P, Methyl 5-chloro-2-[(3-chlorophenoxy)methyl]benzoate 868635-78-3P, 5-Chloro-2-[(3-chlorophenoxy)methyl]benzoic acid 868635-79-4P, Methyl 4-[(1S)-1-[[[5-chloro-2-[(3-chlorophenoxy)methyl]benzoyl]amino]ethyl]benzoate 868635-81-8P, Methyl 5-chloro-2-[(4-chlorophenoxy)methyl]benzoate 868635-82-9P, 5-Chloro-2-[(4-chlorophenoxy)methyl]benzoic acid 868635-83-0P, Methyl 4-[(1S)-1-[[[5-chloro-2-[(4-chlorophenoxy)methyl]benzoyl]amino]ethyl]benzoate 868635-85-2P, Methyl 5-chloro-2-[(4-fluorophenoxy)methyl]benzoate 868635-86-3P, 5-Chloro-2-[(4-fluorophenoxy)methyl]benzoic acid 868635-87-4P, Methyl 4-[(1S)-1-[[[5-chloro-2-[(4-fluorophenoxy)methyl]benzoyl]amino]ethyl]benzoate 868635-89-6P, Methyl 5-chloro-2-[(3-fluorophenoxy)methyl]benzoate 868635-90-9P, 5-Chloro-2-[(3-fluorophenoxy)methyl]benzoic acid 868635-91-0P, Methyl 4-[(1S)-1-[[[5-chloro-2-[(3-fluorophenoxy)methyl]benzoyl]amino]ethyl]benzoate 868635-93-2P, Methyl 5-chloro-2-[(2-fluorophenoxy)methyl]benzoate 868635-94-3P, Methyl 4-[(1S)-1-[[[5-chloro-2-[(2-fluorophenoxy)methyl]benzoyl]amino]ethyl]benzoate 868635-95-4P, 5-Chloro-2-[(2-fluorophenoxy)methyl]benzoic acid 868635-97-6P, Methyl 5-chloro-2-[(2,3-difluorophenoxy)methyl]benzoate 868635-98-7P, 5-Chloro-2-[(2,3-difluorophenoxy)methyl]benzoic acid 868635-99-8P, Methyl 4-[(1S)-1-[[[5-chloro-2-[(2,3-difluorophenoxy)methyl]benzoyl]amino]ethyl]benzoate 868636-01-5P, Methyl 5-chloro-2-[(2,4-difluorophenoxy)methyl]benzoate 868636-03-7P, 5-Chloro-2-[(2,4-difluorophenoxy)methyl]benzoic acid 868636-05-9P, Methyl 4-[(1S)-1-[[[5-chloro-2-[(2,4-difluorophenoxy)methyl]benzoyl]amino]ethyl]benzoate 868636-09-3P, Methyl 5-chloro-2-[(2,5-difluorophenoxy)methyl]benzoate 868636-11-7P, 5-Chloro-2-[(2,5-difluorophenoxy)methyl]benzoic acid 868636-13-9P, Methyl 4-[(1S)-1-[[[5-chloro-2-[(2,5-difluorophenoxy)methyl]benzoyl]amino]ethyl]benzoate 868636-16-2P, Methyl 5-chloro-2-[(2,6-difluorophenoxy)methyl]benzoate 868636-17-3P, 5-Chloro-2-[(2,6-difluorophenoxy)methyl]benzoic acid 868636-18-4P, Methyl 4-[(1S)-1-[[[5-chloro-2-[(2,6-difluorophenoxy)methyl]benzoyl]amino]ethyl]benzoate 868636-20-8P, Methyl 5-chloro-2-[(3,4-difluorophenoxy)methyl]benzoate 868636-21-9P, 5-Chloro-2-[(3,4-difluorophenoxy)methyl]benzoic acid 868636-22-0P, Methyl 4-[(1S)-1-[[[5-chloro-2-[(3,4-difluorophenoxy)methyl]benzoyl]amino]ethyl]benzoate 868636-24-2P, Methyl 5-chloro-2-[(3,5-difluorophenoxy)methyl]benzoate 868636-25-3P, 5-Chloro-2-[(3,5-difluorophenoxy)methyl]benzoic acid 868636-26-4P, Methyl 4-[(1S)-1-[[[5-chloro-2-[(3,5-difluorophenoxy)methyl]benzoyl]amino]ethyl]benzoate 868636-28-6P, Methyl 5-chloro-2-[[[4-methylphenyl]oxy]methyl]benzoate 868636-29-7P, 5-Chloro-2-[[[4-methylphenyl]oxy]methyl]benzoic acid 868636-30-0P, Methyl 4-[(1S)-1-[[[5-chloro-2-[[[4-methylphenyl]oxy]methyl]benzoyl]amino]ethyl]benzoate 868636-32-2P, Methyl 5-chloro-2-[[[5-fluoropyridin-3-yl]oxy]methyl]benzoate 868636-33-3P, 5-Chloro-2-[[[5-fluoropyridin-3-yl]oxy]methyl]benzoic acid 868636-34-4P, Methyl 4-[(1S)-1-[[[5-chloro-2-[[[5-fluoropyridin-3-yl]oxy]methyl]benzoyl]amino]ethyl]benzoate 868636-36-6P, Methyl 5-chloro-2-[[[5-chloropyridin-3-yl]oxy]methyl]benzoate 868636-37-7P, 5-Chloro-2-[[[5-chloropyridin-3-yl]oxy]methyl]benzoic acid 868636-38-8P, Methyl 4-[(1S)-1-[[[5-chloro-2-[[[5-chloropyridin-3-yl]oxy]methyl]benzoyl]amino]ethyl]benzoate

868636-40-2P, 5-Chloro-2-[(cyclopentyloxy)methyl]benzoic acid
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868637-14-3P, Methyl 4-[(1S)-1-[[[5-chloro-2-[methyl(2-phenylethyl)amino]pyridin-3-yl]carbonyl]amino]ethyl]benzoate
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 868637-50-7P, Methyl 4-[(1S)-1-[[[5-chloro-2-[(3,4-difluorobenzyl)oxy]benzoyl]amino]ethyl]benzoate
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(combinations comprising EP4-receptor antagonists and $\alpha 2\delta$ ligands for treating pain)

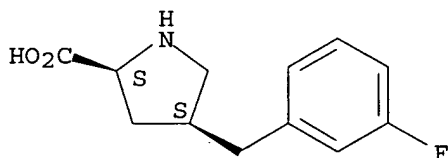
IT **686766-31-4P**, (2S,4S)-4-(3-Fluorobenzyl)pyrrolidine-2-carboxylic acid monohydrochloride **686766-87-0P**, (2S,4S)-4-(3-Chlorophenoxy)pyrrolidine-2-carboxylic acid
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(codrug; combinations comprising EP4-receptor antagonists and $\alpha 2\delta$ ligands for treating pain)

RN 686766-31-4 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, hydrochloride, (4S)- (9CI) (CA INDEX NAME)

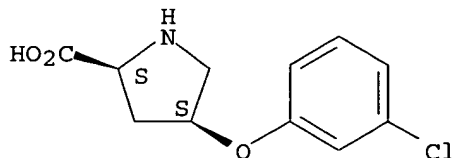
Absolute stereochemistry.



● HCl

RN 686766-87-0 CAPLUS
 CN L-Proline, 4-(3-chlorophenoxy)-, (4S)- (9CI) (CA INDEX NAME)

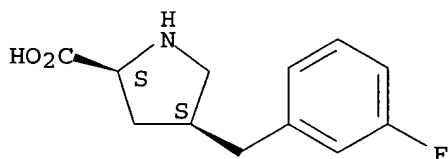
Absolute stereochemistry.



IT 688007-58-1
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (codrug; combinations comprising EP4-receptor antagonists and $\alpha 2\delta$ ligands for treating pain)

RN 688007-58-1 CAPLUS
 CN L-Proline, 4-[(3-fluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

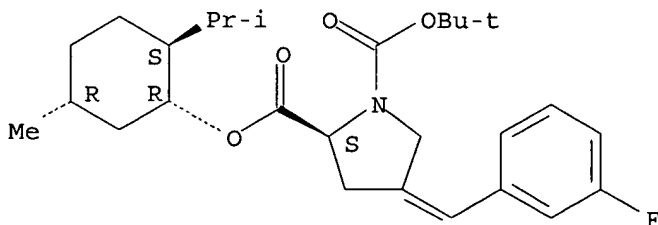
Absolute stereochemistry.



IT 686766-69-8
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (combinations comprising EP4-receptor antagonists and $\alpha 2\delta$ ligands for treating pain)

RN 686766-69-8 CAPLUS
 CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methylene]-, 1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl] ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.



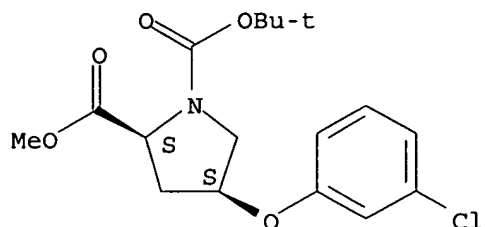
IT 686766-55-2P, (2S,4S)-4-(3-Chlorophenoxy)pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester 686766-56-3P
 686766-74-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (combinations comprising EP4-receptor antagonists and $\alpha 2\delta$ ligands for treating pain)

RN 686766-55-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3-chlorophenoxy)-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

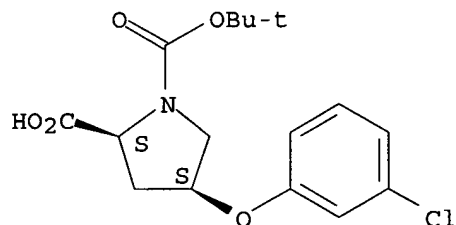
Absolute stereochemistry.



RN 686766-56-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3-chlorophenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

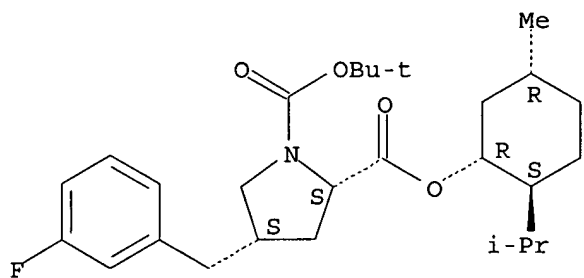
Absolute stereochemistry.



RN 686766-74-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methyl]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L46 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1123883 CAPLUS

DOCUMENT NUMBER: 143:387378

TITLE: Process for the recrystallization of proline
derivatives.

INVENTOR(S): Warren, Andrew Nicholas

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 15 pp.

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005097741	A1	20051020	WO 2005-IB889	20050330
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

GB 2004-7731

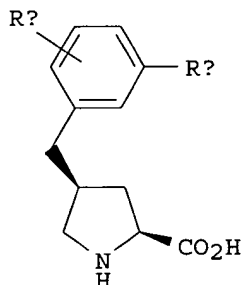
A. 20040405

US 2004-571786P

P 20040517

OTHER SOURCE(S):
GI

MARPAT 143:387378



Good date

AB The invention relates to a process for the preparation of benzylpyrrolidine-2-carboxylic acid derivs. I [Ra, Rb are independently H, halo, OH, CN, NO₂, alkyl, alkoxy, alkylamino, acyl, alkylthio, alkylaminosulfonyl, cycloalkyl, heterocycloalkyl, Ph, heteroaryl, etc., with the provisos that R₁ = R_b ≠ H, when R_b is a para substituent, R_a ≠ H, and when R_a is MeO, R_b ≠ H] or their pharmaceutically-acceptable salts in essentially diastereomerically pure form by recrystn. from aqueous acetonitrile. Thus, (2S)-4-(3-fluorobenzyl)pyrrolidine-1,2-dicarboxylic acid 1-tert-Bu ester 2-Me ester was prepared and heated to reflux in M HCl. Recrystn. of the product from MeCN-water (95:5 by volume) afforded I (R_a = F, R_b = H) as a single diastereomer.

IC ICM C07D207-16

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 75

IT 686766-31-4P 688007-58-1P

RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
 (recrystn. of benzylproline derivs.)

IT 686766-59-6 686766-69-8

RL: RCT (Reactant); RACT (Reactant or reagent)
(recrystn. of benzylproline derivs.)

IT **866488-98-4P 866489-00-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(recrystn. of benzylproline derivs.)

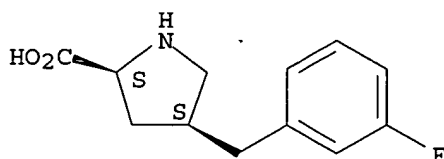
IT **686766-31-4P 688007-58-1P**

RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN
(Synthetic preparation); PREP (Preparation)
(recrystn. of benzylproline derivs.)

RN 686766-31-4 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, hydrochloride, (4S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

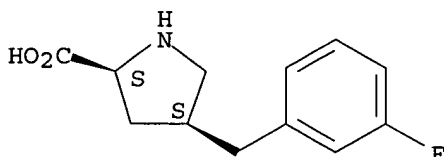


● HCl

RN 688007-58-1 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **686766-59-6 686766-69-8**

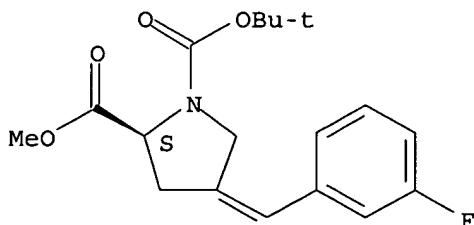
RL: RCT (Reactant); RACT (Reactant or reagent)
(recrystn. of benzylproline derivs.)

RN 686766-59-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methylene]-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

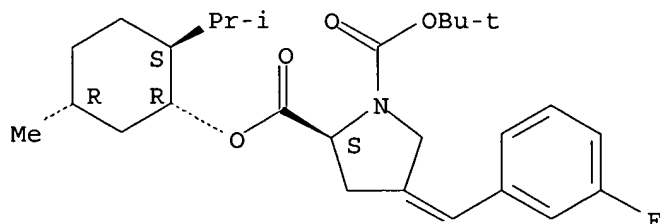
Double bond geometry unknown.



RN 686766-69-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methylene]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



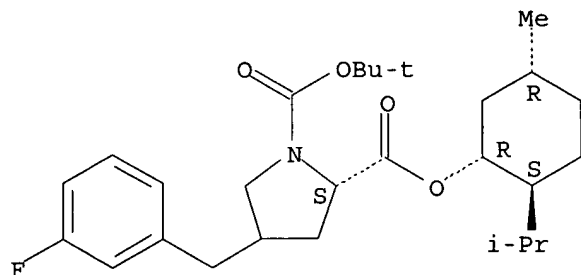
IT 866488-98-4P 866489-00-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(recrystn. of benzylproline derivs.)

RN 866488-98-4 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methyl]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S)- (9CI) (CA INDEX NAME)

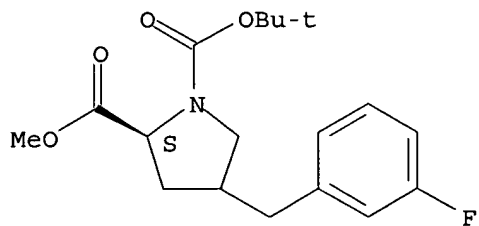
Absolute stereochemistry.



RN 866489-00-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methyl]-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1075617 CAPLUS
DOCUMENT NUMBER: 143:367000
TITLE: Preparation of atypical antipsychotics for combinations with α -2-8 ligands
INVENTOR(S): Field, Mark John; Williams, Richard Griffith
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005092318	A1	20051006	WO 2005-IB510	20050224
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.:

GB 2004-5200 A 20040308
US 2004-560416P P 20040407

AB The instant invention relates to a combination, particularly a synergistic combination, of an α -2-8 ligand and an atypical antipsychotic, and pharmaceutically acceptable salts thereof, pharmaceutical compns. thereof and their use in the treatment of pain, particularly neuropathic pain. (3R,4R,5R)-3-amino-4,5-dimethylheptanoic acid, an atypical antipsychotic, was prepared via a series of reactions starting with (S)-3-[(E)-2-methylpent-2-enoyl]-4-phenyloxazolidin-2-one. Example α -2-8 ligands include gabapentin.

IC ICM A61K031-197

ICS A61K031-401; A61K031-411; A61K031-496; A61K031-551; A61K031-5513; A61K031-517; A61K031-554; A61P025-00

CC 23-16 (Aliphatic Compounds)

Section cross-reference(s): 1, 28, 63

IT 60142-96-3, Gabapentin 146939-27-7, Ziprasidone 148553-50-8, Pregabalin 223445-75-8 227625-35-6 313651-33-1 335458-65-6 473924-33-3 610300-07-7 610300-19-1 610300-20-4 686766-87-0 688007-58-1 866108-70-5

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preparation of atypical antipsychotics for combinations with α -2-8 ligands)

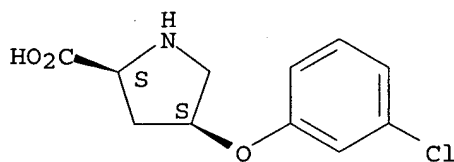
IT 686766-87-0 688007-58-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preparation of atypical antipsychotics for combinations with α -2-8 ligands)

RN 686766-87-0 CAPLUS

CN L-Proline, 4-(3-chlorophenoxy)-, (4S)- (9CI) (CA INDEX NAME)

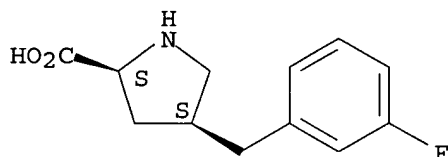
Absolute stereochemistry.



RN 688007-58-1 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:493505 CAPLUS

DOCUMENT NUMBER: 143:32337

TITLE: Calcium carbonate for stabilizing solid pharmaceutical compositions of amino acids

INVENTOR(S): Razzano, Elena

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051384	A1	20050609	WO 2004-IB3743	20041112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

GB 2003-27389

A 20031125

US 2004-535845P

P 20040112

OTHER SOURCE(S): MARPAT 143:32337

AB The present invention relates to the use of calcium carbonate as a stabilizing agent in solid pharmaceutical compns. comprising an amino acid as the pharmaceutically active agent, to the stabilized pharmaceutical compns. resulting therefrom and processes for their preparation Thus, tablets were prepared containing (+)-(2S)-5-amino-2-[(1-n-propyl-1H-imidazol-4-

yl)methyl]pentanoic acid (active component) 31.13 mg, microcryst. cellulose 32.31 mg, calcium carbonate 32.31 mg, croscarmellose sodium 3.00 mg, and magnesium stearate 1.25 mg. Tablets stored at 40° and 75% relative humidity for 12 wk showed the presence of 98.9% of the active component.

IC ICM A61K031-41

CC 63-6 (Pharmaceuticals)

IT 60142-96-3, 1-(Aminomethyl)cyclohexaneacetic acid 148553-50-8
 313651-33-1, (3S,5R)-3-Aminomethyl-5-methyloctanoic acid 400044-42-0
 400044-45-3 400044-47-5 400044-49-7 400044-64-6 400044-71-5
 400044-72-6 473829-37-7 473829-38-8 473829-39-9 473829-40-2
 473829-41-3 473829-42-4 473829-43-5 473829-44-6 473829-45-7
 473829-46-8 473829-47-9 473924-33-3 473924-35-5 497158-84-6
 497158-85-7 497158-86-8 497158-87-9 570397-64-7 570397-73-8
 570397-75-0 570398-09-3 570399-68-7 570399-69-8 570399-70-1

686766-37-0 686766-38-1 686766-43-8

686766-44-9 686766-87-0 688007-60-5

852921-29-0 852921-30-3 852921-31-4

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(calcium carbonate stabilization of amino acid-containing solid dosage forms)

IT 686766-37-0 686766-38-1 686766-43-8

686766-44-9 686766-87-0 688007-60-5

852921-29-0 852921-30-3 852921-31-4

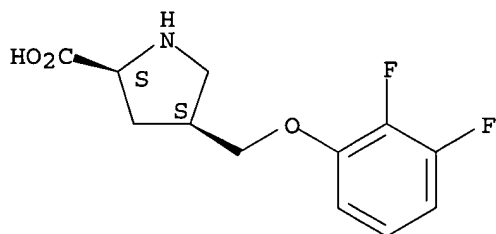
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(calcium carbonate stabilization of amino acid-containing solid dosage forms)

RN 686766-37-0 CAPLUS

CN L-Proline, 4-[(2,3-difluorophenoxy)methyl]-, (4S)- (9CI) (CA INDEX NAME)

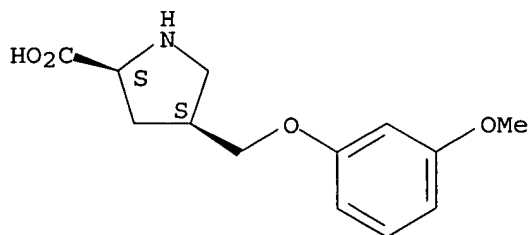
Absolute stereochemistry.



RN 686766-38-1 CAPLUS

CN L-Proline, 4-[(3-methoxyphenoxy)methyl]-, (4S)- (9CI) (CA INDEX NAME)

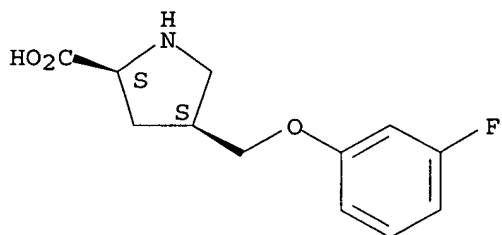
Absolute stereochemistry.



RN 686766-43-8 CAPLUS

CN L-Proline, 4-[(3-fluorophenoxy)methyl]-, (4S)- (9CI) (CA INDEX NAME)

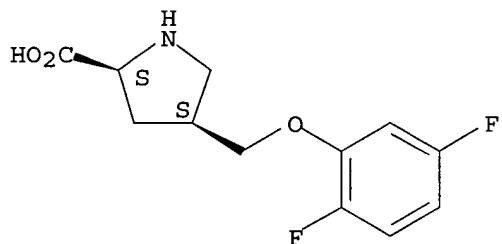
Absolute stereochemistry.



RN 686766-44-9 CAPLUS

CN L-Proline, 4-[(2,5-difluorophenoxy)methyl]-, (4S)- (9CI) (CA INDEX NAME)

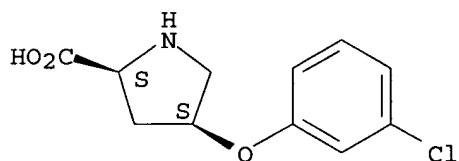
Absolute stereochemistry.



RN 686766-87-0 CAPLUS

CN L-Proline, 4-(3-chlorophenoxy)-, (4S)- (9CI) (CA INDEX NAME)

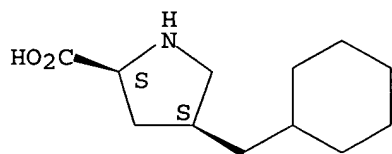
Absolute stereochemistry.



RN 688007-60-5 CAPLUS

CN L-Proline, 4-(cyclohexylmethyl)-, (4S)- (9CI) (CA INDEX NAME)

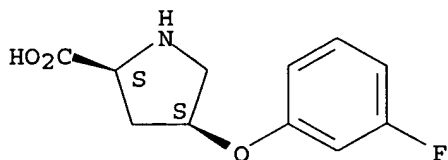
Absolute stereochemistry. Rotation (-).



RN 852921-29-0 CAPLUS

CN L-Proline, 4-(3-fluorophenoxy)-, (4S)- (9CI) (CA INDEX NAME)

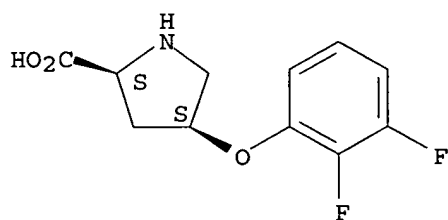
Absolute stereochemistry.



RN 852921-30-3 CAPLUS

CN L-Proline, 4-(2,3-difluorophenoxy)-, (4S)- (9CI) (CA INDEX NAME)

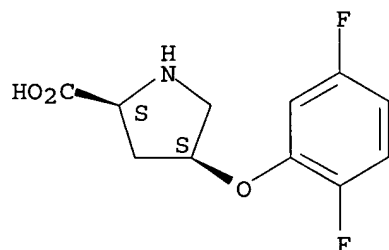
Absolute stereochemistry.



RN 852921-31-4 CAPLUS

CN L-Proline, 4-(2,5-difluorophenoxy)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:531356 CAPLUS

DOCUMENT NUMBER: 141:65106

TITLE: Calcium channel α -2- δ subunit ligands to treat chronic obstructive pulmonary disease (COPD), chronic cough, and other diseases

INVENTOR(S): Bertrand, Claude Philippe; Chovet, Maria Emilia Pereira Chicau; Geppetti, Pierangelo; Taylor, Charles Price, Jr.; Thorpe, Andrew John; Wustrow, David Juergen

PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 9
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054577	A1	20040701	WO 2003-IB5640	20031203
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2451267	AA	20040613	CA 2003-2451267	20031127
US 2004176456	A1	20040909	US 2003-726878	20031202
US 2004132636	A1	20040708	US 2003-731605	20031209
US 2004180958	A1	20040916	US 2003-732613	20031210
US 2004143014	A1	20040722	US 2003-735398	20031212
PRIORITY APPLN. INFO.:			US 2002-433491P	P 20021213
			GB 2003-2657	A 20030205
			US 2003-454074P	P 20030312

OTHER SOURCE(S): MARPAT 141:65106

AB The invention discloses the use of an calcium channel α -2-8 subunit ligand in the treatment of chronic obstructive pulmonary disease (COPD) and diseases associated with a diagnosis of COPD, and particularly to the treatment of chronic cough, which may be unrelated to COPD. Compound preparation is included.

IC ICM A61K031-4245

ICS A61K031-195; A61K031-197; A61K031-401; A61P011-00; A61P011-14

CC 1-9 (Pharmacology)

Section cross-reference(s): 27

IT 686766-31-4P 686766-32-5P 686766-43-8P

686766-87-0P 713077-39-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(calcium channel α -2-8 subunit ligands to treat chronic obstructive pulmonary disease, chronic cough, and other diseases)

IT 60142-96-3, Gabapentin 223445-75-8 227625-35-6 313651-33-1

335458-65-6 473924-33-3 610300-07-7 610300-19-1 610300-20-4

686766-42-7 688007-58-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(calcium channel α -2-8 subunit ligands to treat chronic obstructive pulmonary disease, chronic cough, and other diseases)

IT 108-43-0, 3-Chlorophenol 74844-91-0 344286-69-7 686766-74-5

713077-38-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(calcium channel α -2-8 subunit ligands to treat chronic obstructive pulmonary disease, chronic cough, and other diseases)

IT 686766-55-2P 686766-56-3P 686766-69-8P

686766-82-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(calcium channel α -2-8 subunit ligands to treat chronic obstructive pulmonary disease, chronic cough, and other diseases)

IT 686766-31-4P 686766-32-5P 686766-43-8P

686766-87-0P 713077-39-5P

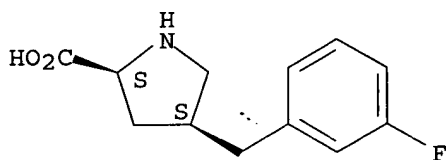
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(calcium channel α -2- δ subunit ligands to treat chronic obstructive pulmonary disease, chronic cough, and other diseases)

RN 686766-31-4 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, hydrochloride, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

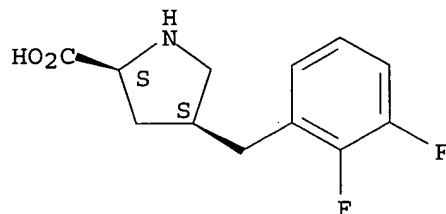


● HCl

RN 686766-32-5 CAPLUS

CN L-Proline, 4-[(2,3-difluorophenyl)methyl]-, hydrochloride, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

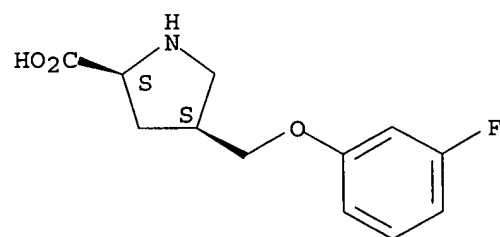


● HCl

RN 686766-43-8 CAPLUS

CN L-Proline, 4-[(3-fluorophenoxy)methyl]-, (4S)- (9CI) (CA INDEX NAME)

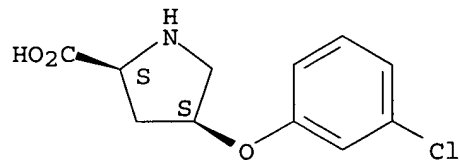
Absolute stereochemistry.



RN 686766-87-0 CAPLUS

CN L-Proline, 4-(3-chlorophenoxy)-, (4S)- (9CI) (CA INDEX NAME)

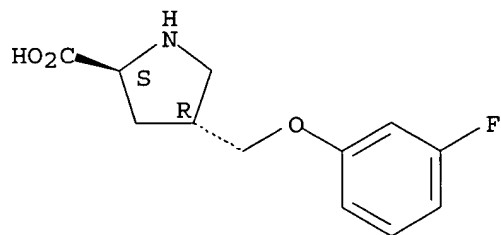
Absolute stereochemistry.



RN 713077-39-5 CAPLUS

CN L-Proline, 4-[(3-fluorophenoxy)methyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 686766-42-7 688007-58-1

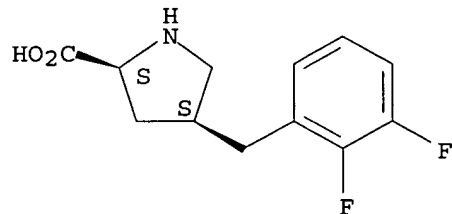
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(calcium channel α -2-8 subunit ligands to treat chronic obstructive pulmonary disease, chronic cough, and other diseases)

RN 686766-42-7 CAPLUS

CN L-Proline, 4-[(2,3-difluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

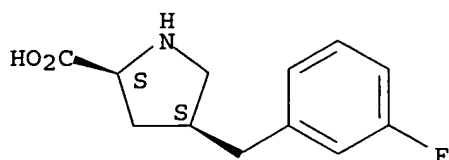
Absolute stereochemistry.



RN 688007-58-1 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



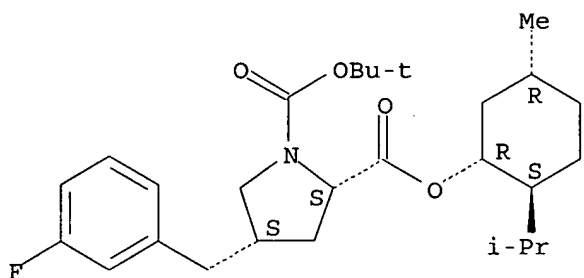
IT 686766-74-5 713077-38-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(calcium channel α -2- δ subunit ligands to treat chronic
obstructive pulmonary disease, chronic cough, and other diseases)

RN 686766-74-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methyl]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S,4S)- (9CI) (CA INDEX NAME)

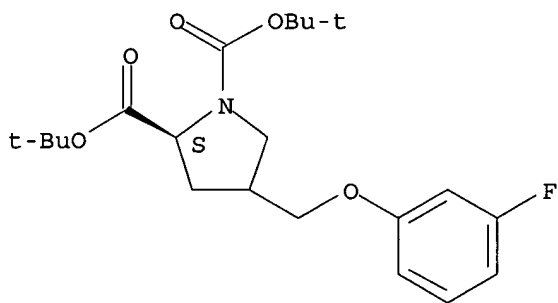
Absolute stereochemistry.



RN 713077-38-4 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenoxy)methyl]-,
bis(1,1-dimethylethyl) ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



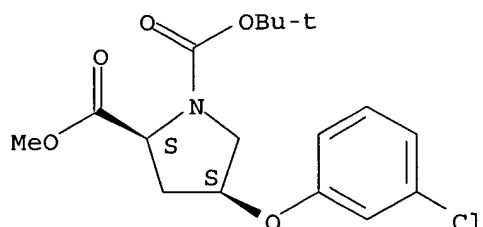
IT 686766-55-2P 686766-56-3P 686766-69-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(calcium channel α -2- δ subunit ligands to treat chronic
obstructive pulmonary disease, chronic cough, and other diseases)

RN 686766-55-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3-chlorophenoxy)-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

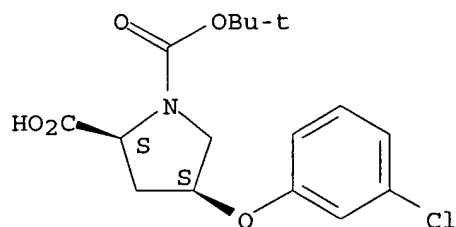
Absolute stereochemistry.



RN 686766-56-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3-chlorophenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

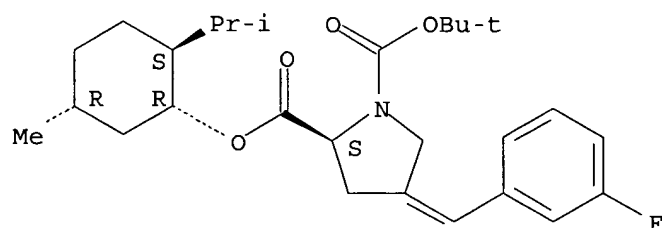
Absolute stereochemistry.



RN 686766-69-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methylene]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:531342 CAPLUS

DOCUMENT NUMBER: 141:88858

TITLE: A preparation of aminocarboxylic acid derivatives as
alpha-2-delta ligands, useful for the treatment of
sexual dysfunction

INVENTOR(S): Taylor, Charles Price, Jr; Thorpe, Andrew John; Van
Der Graaf, Pieter Hadewijn; Wayman, Christopher Peter;
Wustrow, David Juergen

PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

9

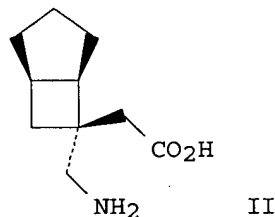
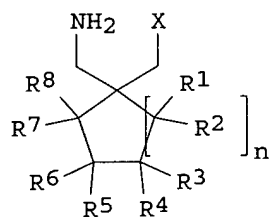
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054563	A1	20040701	WO 2003-IB5682	20031203
W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UY, VC, VN, YU, ZA, ZM, ZW	
RW:			BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG	
CA 2451267	AA	20040613	CA 2003-2451267	20031127
US 2004176456	A1	20040909	US 2003-726878	20031202
CA 2509611	AA	20040701	CA 2003-2509611	20031203
EP 1572183	A1	20050914	EP 2003-775689	20031203
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK	
BR 2003016753	A	20051025	BR 2003-16753	20031203
US 2004132636	A1	20040708	US 2003-731605	20031209
US 2004180958	A1	20040916	US 2003-732613	20031210
US 2004143014	A1	20040722	US 2003-735398	20031212
PRIORITY APPLN. INFO.:			US 2002-433491P	P 20021213
			GB 2003-2657	A 20030205
			US 2003-454074P	P 20030312
			WO 2003-IB5682	W 20031203

OTHER SOURCE(S):

MARPAT 141:88858

GI



AB The invention relates to a preparation of aminocarboxylic acid derivs., e.g. I [wherein: R1, R2, R3, R4, R5, R6, R7, and R8 are independently selected from H or C1-6alkyl, or R8 and R6 or R6 and R4 are taken together to form C3-7 cycloalkyl ring, etc.; n = 0-2; X is a carboxylic acid or carboxylic acid bioisostere], as alpha-2-delta ligands, useful for the treatment of premature ejaculation. For instance, delayed ejaculation in the presence of alpha-2-delta ligand II and effect of compound II on copulatory behavior in rapid ejaculating rats were demonstrated. Compound II increased ejaculation latency by 58% in rapidly ejaculating conscious rats.

IC ICM A61K031-195

ICS A61K031-197; A61K031-4015; A61P015-00

CC 23-16 (Aliphatic Compounds)

Section cross-reference(s): 1, 63

IT **686766-31-4P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aminocarboxylic acid derivs. as alpha-2-delta ligands, useful for the treatment of sexual dysfunction)

IT 60142-96-3P, Gabapentin 148553-50-8P 219135-98-5P 227625-35-6P
227626-51-9P 313651-33-1P 473829-37-7P 473829-38-8P 473829-39-9P
473829-40-2P 473829-41-3P 473829-42-4P 473829-43-5P 473829-44-6P
473829-45-7P 473829-46-8P 473924-33-3P 473924-35-5P 610300-19-1P
686766-30-3P 686766-32-5P 686766-36-9P
686766-42-7P 686766-43-8P 686766-87-0P
688007-58-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminocarboxylic acid derivs. as alpha-2-delta ligands, useful for the treatment of sexual dysfunction)

IT 108-43-0, 3-Chlorophenol 74844-91-0 344286-69-7 **686766-69-8**
686766-81-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminocarboxylic acid derivs. as alpha-2-delta ligands, useful for the treatment of sexual dysfunction)

IT **686766-55-2P 686766-56-3P 686766-74-5P**
686766-76-7P 686766-82-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminocarboxylic acid derivs. as alpha-2-delta ligands, useful for the treatment of sexual dysfunction)

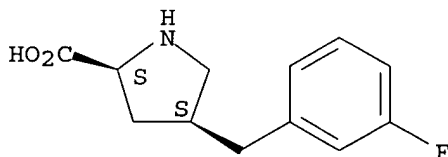
IT **686766-31-4P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aminocarboxylic acid derivs. as alpha-2-delta ligands, useful for the treatment of sexual dysfunction)

RN 686766-31-4 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, hydrochloride, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IT **686766-30-3P 686766-32-5P 686766-36-9P**
686766-42-7P 686766-43-8P 686766-87-0P
688007-58-1P

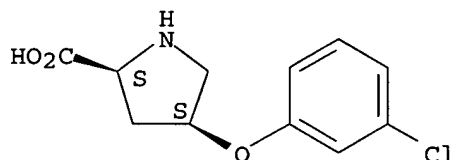
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aminocarboxylic acid derivs. as alpha-2-delta ligands,
useful for the treatment of sexual dysfunction)

RN 686766-30-3 CAPLUS

CN L-Proline, 4-(3-chlorophenoxy)-, hydrochloride, (4S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

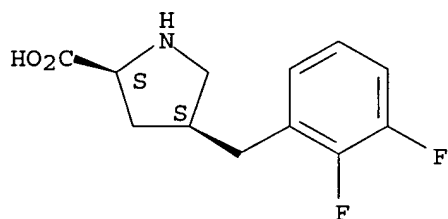


● HCl

RN 686766-32-5 CAPLUS

CN L-Proline, 4-[(2,3-difluorophenyl)methyl]-, hydrochloride, (4S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

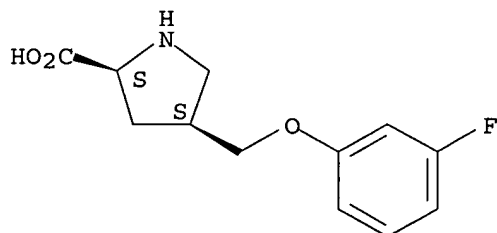


● HCl

RN 686766-36-9 CAPLUS

CN L-Proline, 4-[(3-fluorophenoxy)methyl]-, hydrochloride, (4S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

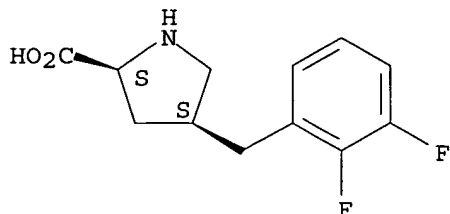


● HCl

RN 686766-42-7 CAPLUS

CN L-Proline, 4-[(2,3-difluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

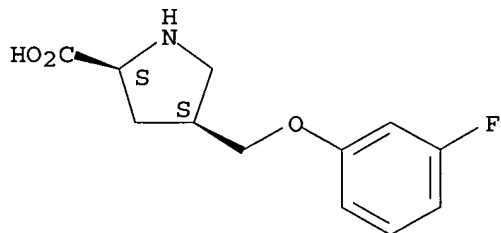
Absolute stereochemistry.



RN 686766-43-8 CAPLUS

CN L-Proline, 4-[(3-fluorophenoxy)methyl]-, (4S)- (9CI) (CA INDEX NAME)

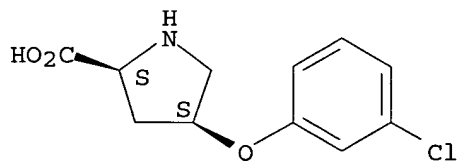
Absolute stereochemistry.



RN 686766-87-0 CAPLUS

CN L-Proline, 4-(3-chlorophenoxy)-, (4S)- (9CI) (CA INDEX NAME)

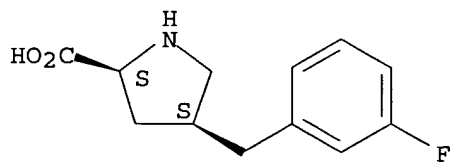
Absolute stereochemistry.



RN 688007-58-1 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 686766-69-8 686766-81-4

RL: RCT (Reactant); RACT (Reactant or reagent)

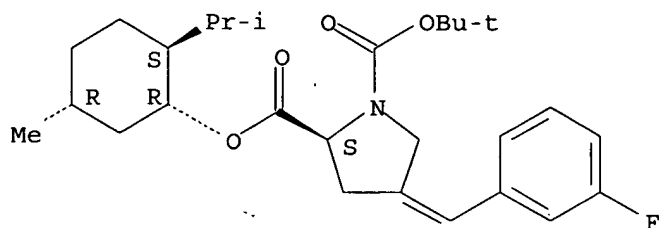
(preparation of aminocarboxylic acid derivs. as alpha-2-delta ligands,
useful for the treatment of sexual dysfunction)

RN 686766-69-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methylene]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

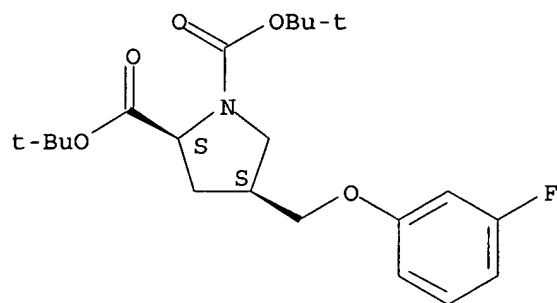
Double bond geometry unknown.



RN 686766-81-4 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenoxy)methyl]-,
bis(1,1-dimethylethyl) ester, (2S,4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 686766-55-2P 686766-56-3P 686766-74-5P
686766-76-7P

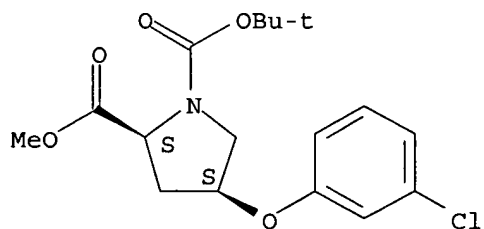
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of aminocarboxylic acid derivs. as alpha-2-delta ligands,
useful for the treatment of sexual dysfunction)

RN 686766-55-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3-chlorophenoxy)-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S,4S)-(9CI) (CA INDEX NAME)

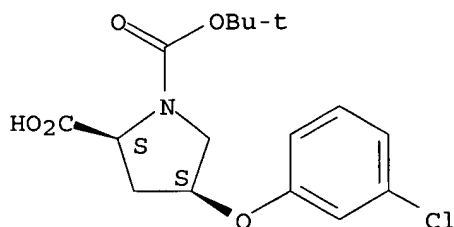
Absolute stereochemistry.



RN 686766-56-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3-chlorophenoxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

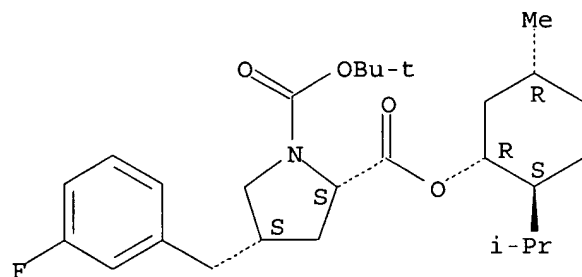
Absolute stereochemistry.



RN 686766-74-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methyl]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S,4S)- (9CI) (CA INDEX NAME)

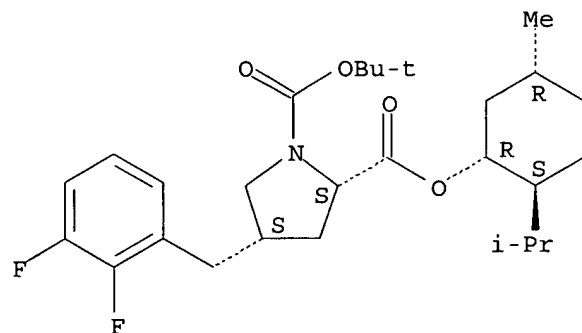
Absolute stereochemistry.



RN 686766-76-7 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,3-difluorophenyl)methyl]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:531340 CAPLUS

DOCUMENT NUMBER: 141:89004

TITLE: Use of alpha-2-delta ligands to treat lower urinary tract symptoms associated with overactive bladder or benign prostatic hyperplasia, and the preparation of 4-substituted pyrrolidine-2-carboxylic acid derivatives and other compounds as ligands for such use

INVENTOR(S): Taylor, Charles Price, Jr.; Thorpe, Andrew John; Westbrook, Simon Lempriere; Wustrow, David Juergen

PATENT ASSIGNEE(S): Warner-Lambert Company Llc, USA

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

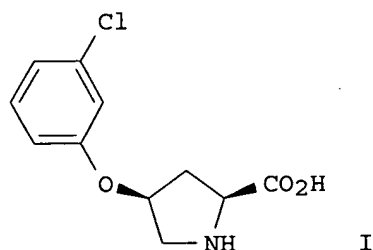
LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054560	A1	20040701	WO 2003-IB5729	20031203
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2509605	AA	20040701	CA 2003-2509605	20031203
EP 1572173	A1	20050914	EP 2003-813233	20031203
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
BR 2003016572	A	20051004	BR 2003-16572	20031203
US 2004180958	A1	20040916	US 2003-732613	20031210
NO 2005003355	A	20050711	NO 2005-3355	20050711
PRIORITY APPLN. INFO.:			US 2002-433491P	P 20021213
			GB 2003-2657	A 20030205
			US 2003-454074P	P 20030312
			WO 2003-IB5729	W 20031203

OTHER SOURCE(S): MARPAT 141:89004
GI



AB Disclosed is the use of an alpha-2-delta ligand, or a pharmaceutically

acceptable derivative thereof, for the manufacture of a medicament for the treatment of lower urinary tract symptoms (LUTS), other than urinary incontinence, which are associated with overactive bladder (OAB) and/or benign prostatic hyperplasia (BPH). Such use of approx. 35 specific compds. and/or their derivs. is claimed. For instance, (2S,4R)-4-hydroxypyrrolidine-1,2-dicarboxylic acid 1-tert-Bu 2-Me ester was etherified with 3-chlorophenol under Mitsunobu conditions (86%), followed by saponification of the Me ester with LiOH in aqueous THF (98%), and hydrolysis of the tert-Bu ester with HCl in dioxane/THF (86.7%), to give acid I, a use-claimed ligand, as the HCl salt, on a 7-kg scale. In tests of gabapentin, a well-known alpha-2-delta ligand, on the micturition reflex of anesthetized rats, a significant, dose-dependent increase in interval between voiding episodes was observed relative to control animals, with a reduction in voids per h from approx. 5 to <1.

IC ICM A61K031-00

ICS A61K031-197; A61P013-00; A61K031-195

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 63

IT **686766-30-3P 686766-87-0P**

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug use candidate; preparation of alpha-2-delta ligands to treat lower urinary tract symptoms)

IT 610300-00-0P 610300-01-1P 610300-02-2P 610300-19-1P

686766-31-4P 686766-32-5P 686766-36-9P

686766-42-7P 688007-58-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug use candidate; preparation of alpha-2-delta ligands to treat lower urinary tract symptoms)

IT **686766-55-2P 686766-56-3P**

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of alpha-2-delta ligands to treat lower urinary tract symptoms)

IT 52745-93-4P, (R)-4-Methylhexanoic acid 53353-03-0P, (R)-2,6-Dimethyloct-

2-ene 115109-01-8P 128342-71-2P 208836-20-8P 313653-09-7P

313653-10-0P 313653-11-1P 313653-16-6P, Methanesulfonic acid

(S)-3,7-dimethyloct-6-enyl ester 313653-17-7P 313653-18-8P

313653-19-9P 313653-37-1P 313653-38-2P 313653-39-3P 610300-35-1P

610300-36-2P 610300-37-3P 610300-38-4P 610300-39-5P 610300-40-8P

686766-74-5P 686766-76-7P 686766-82-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of alpha-2-delta ligands to treat lower urinary tract symptoms)

IT 100-51-6, Benzyl alcohol, reactions 108-43-0, 3-Chlorophenol

5292-43-3, tert-Butyl bromoacetate 7540-51-4, (S)-Citronellol

74844-91-0 77943-39-6, (4R,5S)-(+)-4-Methyl-5-phenyl-2-oxazolidinone

143615-81-0, (S)-Citronellyl bromide 344286-69-7 **686766-69-8**

686766-71-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(starting material; preparation of alpha-2-delta ligands to treat lower urinary tract symptoms)

IT **686766-30-3P 686766-87-0P**

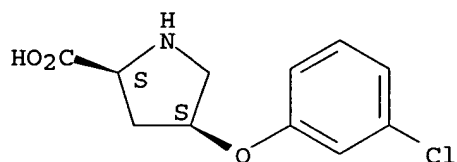
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug use candidate; preparation of alpha-2-delta ligands to treat lower urinary tract symptoms)

RN 686766-30-3 CAPLUS

CN L-Proline, 4-(3-chlorophenoxy)-, hydrochloride, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

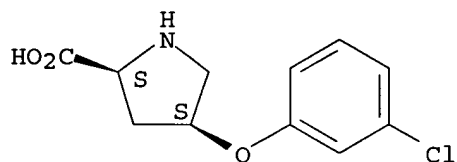


● HCl

RN 686766-87-0 CAPLUS

CN L-Proline, 4-(3-chlorophenoxy)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 686766-31-4P 686766-32-5P 686766-36-9P
686766-42-7P 688007-58-1P

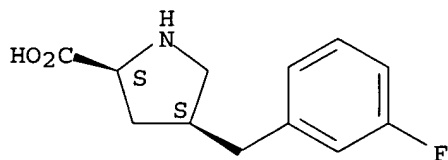
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug use candidate; preparation of alpha-2-delta ligands to treat lower urinary tract symptoms)

RN 686766-31-4 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, hydrochloride, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



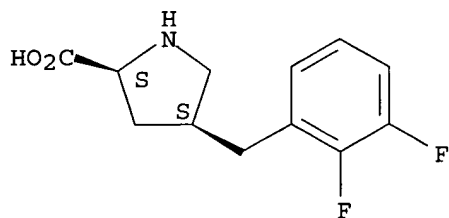
● HCl

RN 686766-32-5 CAPLUS

CN L-Proline, 4-[(2,3-difluorophenyl)methyl]-, hydrochloride, (4S)- (9CI)

(CA INDEX NAME)

Absolute stereochemistry.

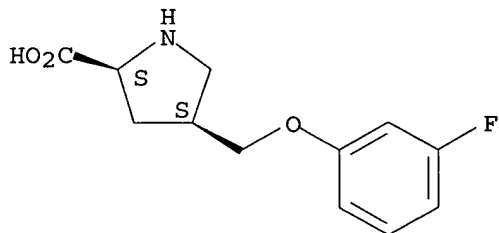


● HCl

RN 686766-36-9 CAPLUS

CN L-Proline, 4-[(3-fluorophenoxy)methyl]-, hydrochloride, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

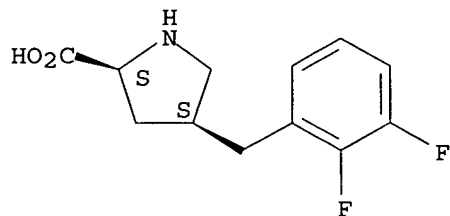


● HCl

RN 686766-42-7 CAPLUS

CN L-Proline, 4-[(2,3-difluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

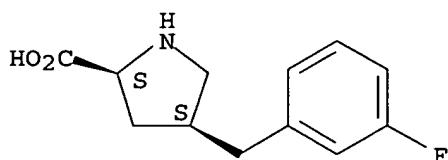
Absolute stereochemistry.



RN 688007-58-1 CAPLUS

CN L-Proline, 4-[(3-fluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



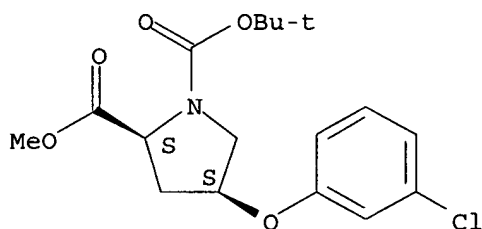
IT 686766-55-2P 686766-56-3P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of alpha-2-delta ligands to treat lower urinary tract symptoms)

RN 686766-55-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3-chlorophenoxy)-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

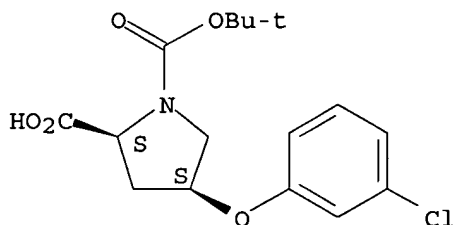
Absolute stereochemistry.



RN 686766-56-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3-chlorophenoxy)-, 1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



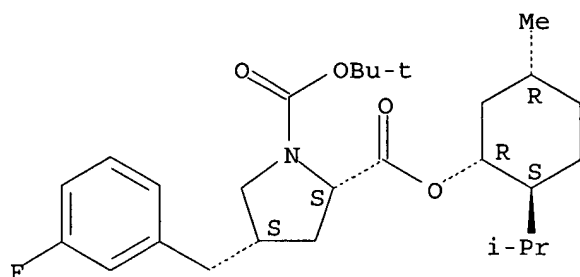
IT 686766-74-5P 686766-76-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of alpha-2-delta ligands to treat lower urinary tract symptoms)

RN 686766-74-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methyl]-, 1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl] ester, (2S,4S)- (9CI) (CA INDEX NAME)

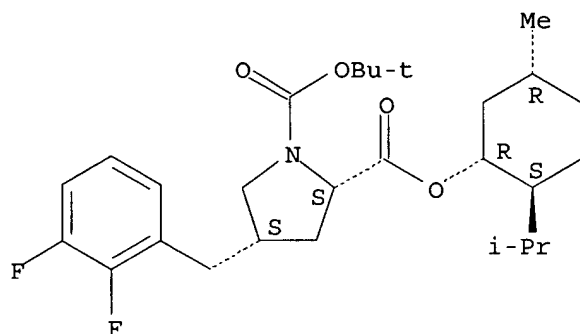
Absolute stereochemistry.



RN 686766-76-7 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,3-difluorophenyl)methyl]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 686766-69-8 686766-71-2

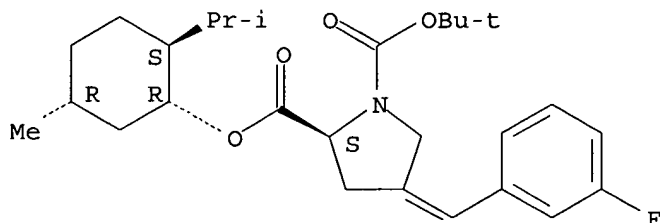
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of alpha-2-delta ligands to treat lower
urinary tract symptoms)

RN 686766-69-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-fluorophenyl)methylene]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

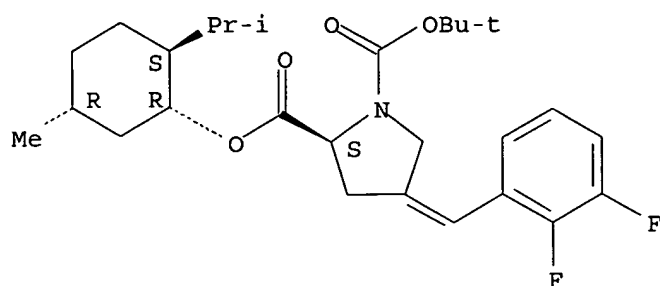
Double bond geometry unknown.



RN 686766-71-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,3-difluorophenyl)methylene]-,
1-(1,1-dimethylethyl) 2-[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]
ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L1	STR
L4	1152 SEA FILE=REGISTRY SSS FUL L1
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L24	71 SEA FILE=CAPLUS ABB=ON PLU=ON L23

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L47 61 L24 NOT (L45 OR L46)

=> d ibib abs hitind hitstr L47 1-61

L47 ANSWER 1 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1220126 CAPLUS

DOCUMENT NUMBER: 143:477844

TITLE: Preparation of acylated 2-amino-1-(pyrrolidin-2-yl)ethanols and derivatives as BACE inhibitors for treating Alzheimer's

INVENTOR(S): Dally, Robert Dean; Shepherd, Timothy Alan; Bender, David Michael; Rojo Garcia, Maria Isabel

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 193 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005108358	A2	20051117	WO 2005-US12191	20050408
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

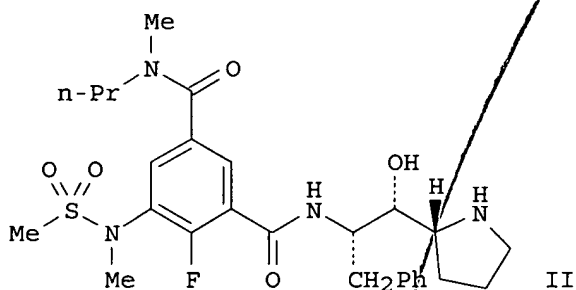
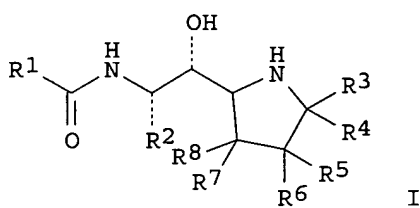
US 2004-564538P

P 20040422

OTHER SOURCE(S):

MARPAT 143:477844

GI



AB Title compds. I [R1 = biphenyl substituted with halo, (un)substituted cycloalkyl/alk(en/yn)yl, cycloalkyl; R2 = alkyl, (un)substituted benzyl; R3 = H, alkyl; R4 = H, alkyl, Ph; R3CR4 = cycloalkyl ring; R5 = H, F, CF3, (un)substituted Ph; R6 = F, OH, OTs, , etc.; R5R6 = :CHC(:O)-alkoxy; R7 = H, F; R6 and R7 taken together for a bond; R8 = H, F; and their pharmaceutically acceptable salts; with provisos] were prepared as β -site APP-cleaving enzyme (BACE) inhibitors. Thus, amidation of 6-Fluoro-5-[(methylsulfonyl) (methyl) amino]-N-methyl-N-propylisophthalamic acid (preparation given) with (R)-2-((1S,2S)-2-Amino-1-hydroxy-3-phenylpropyl)pyrrolidine-1-carboxylic acid tert-Bu ester and Boc-deprotection gave II•HCl. I exhibited an IC₅₀ for BACE1 and BACE2 of at least 15 μ M in a BACE1 and BACE2 mcaFRET assay. Thus, I are useful for treating Alzheimer's disease and preventing progressive of mild cognitive impairment to Alzheimer's disease.

IC ICM C07D207-00

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

IT 1633-84-7P, 4-Chlorobutanesulfonyl chloride 2924-09-6P,
(5-Bromo-2-fluorophenyl)amine 3144-06-7P, 4-Chlorobutanesulfonamide
23351-91-9P, 5-Bromoisophthalic acid 42521-10-8P, 2-Chloro-6-
methoxyisonicotinic acid methyl ester 75308-46-2P, tert-Butyl
2,6-dichloroisonicotinate 89238-99-3P, 2,2,2-Trichloroacetimidic acid
4-methoxybenzyl ester 89469-46-5P, 3-[(Methylsulfonyl)(methyl)amino]benz
oic acid 93116-99-5P, 5-Iodoisophthalic acid monomethyl ester
95798-31-5P, 4-(S)-Isopropyl-3-(3-phenylpropionyl)oxazolidin-2-one
106719-08-8P, 2-Chloro-6-methoxyisonicotinic acid ethyl ester
111060-64-1P, 2-(S)-Dibenzylamino-3-phenylpropionaldehyde 114676-59-4P,
4-(R)-Hydroxypyrrolidine-2-(R)-carboxylic acid methyl ester hydrochloride
114676-69-6P, (2R,4R)-4-Hydroxypyrrolidine-1,2-dicarboxylic acid
1-tert-butyl ester 2-methyl ester 126926-35-0P, N,N-
Dipropylisophthalamide 135042-17-0P, (2R,4S)-4-Hydroxypyrrolidine-
1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester 153203-57-7P,
5-Chloroisophthalic acid monomethyl ester 157224-25-4P,
1,3-Difluoro-5-(2-nitrovinyl)benzene 161796-10-7P, 5-Bromoisophthalic
acid monomethyl ester 178962-09-9P, 4-(S)-Hydroxypyrrolidine-2-(R)-
carboxylic acid methyl ester 180891-39-8P, Cyclopropanesulfonic acid
methylamide 182483-64-3P, 2-Benzyloxy-6-chloroisonicotinic acid methyl
ester 185739-14-4P, Toluene-4-sulfonic acid 2,2-difluorovinyl ester
195447-25-7P, 3,3-Difluoropyrrolidine-1-carboxylic acid tert-butyl ester
250122-38-4P, (2R,4R)-4-Benzyloxypyrrolidine-1,2-dicarboxylic acid
1-tert-butyl ester 2-methyl ester 250122-39-5P, (2R,4R)-4-Benzyloxy-2-
formylpyrrolidine-1-carboxylic acid tert-butyl ester 328284-59-9P,
5-Nitro-N,N-dipropylisophthalamide acid methyl ester 388071-68-9P,
5-Hydroxymethylisophthalic acid monoethyl ester 388072-33-1P,
2-(Dipropylcarbamoyl)isonicotinic acid 480464-82-2P,
5-Isopropoxyisophthalic acid monomethyl ester 480464-83-3P, Dimethyl
5-isopropoxyisophthalate 537658-48-3P, N-Methyl-5-(2-oxopyrrolidin-1-yl)-
N-propylisophthalamide acid methyl ester 537658-49-4P,
N-Methyl-5-(2-oxopyrrolidin-1-yl)-N-propylisophthalamide acid
597561-60-9P, 5-Iodo-N-methyl-N-propylisophthalamide acid methyl ester
597561-61-0P, N-Methyl-5-(oxazol-2-yl)-N-propylisophthalamide acid
597563-35-4P, N-Methyl-N-propyl-5-(thiazol-2-yl)isophthalamide acid methyl
ester 647857-39-4P, 4-(4S)-Fluoropyrrolidine-1,2-(R)-dicarboxylic acid
1-tert-butyl ester 2-methyl ester 647857-43-0P, 4-(R)-Fluoropyrrolidine-
N,2-(R)-dicarboxylic acid 1-tert-butyl ester 2-methyl ester
845543-66-0P, 2-(R)-[2-(S)-Amino-3-(3,5-difluorophenyl)-1-(S)-
hydroxypropyl]pyrrolidine-1-carboxylic acid tert-butyl ester
845546-62-5P, (2R,4R)-2-[(1S,2S)-2-Amino-3-(3,5-difluorophenyl)-1-
hydroxypropyl]-4-benzyloxypyrrolidine-1-carboxylic acid tert-butyl ester
853304-06-0P, 2-Chloro-6-[(methylsulfonyl)(methyl)amino]isonicotinic acid
methyl ester 869527-39-9P, 2-[2-(S)-[Bis(2-methylbenzyl)amino]-3-(3,5-
difluorophenyl)-1-(S)-hydroxypropyl]pyrrole-1-carboxylic acid tert-butyl
ester 869527-41-3P, 2-(R)-[2-(S)-[Bis(2-methylbenzyl)amino]-3-(3,5-
difluorophenyl)-1-(S)-hydroxypropyl]pyrrolidine-1-carboxylic acid
tert-butyl ester 869527-43-5P, 2-(R)-[2-(S)-Dibenzylamino-1-(S)-hydroxy-
3-phenylpropyl]pyrrolidine-1-carboxylic acid tert-butyl ester
869527-44-6P, 2-(R)-[2-(S)-Amino-1-(S)-hydroxy-3-phenylpropyl]-4-(S)-
fluoropyrrolidine-1-carboxylic acid tert-butyl ester 869527-45-7P
869527-46-8P, 4-(S)-Fluoro-2-(R)-hydroxymethylpyrrolidine-1-carboxylic
acid tert-butyl ester 869527-47-9P, 4-(S)-Fluoro-2-(R)-[1-(S)-hydroxy-2-
(S)-nitro-3-phenylpropyl]pyrrolidine-1-carboxylic acid tert-butyl ester
869527-48-0P, 4-(S)-Fluoro-2-(R)-[1-(R)-hydroxy-2-(S)-nitro-3-
phenylpropyl]pyrrolidine-1-carboxylic acid tert-butyl ester
869527-49-1P, 2-(R)-[2-(S)-Amino-1-(S)-hydroxy-3-phenylpropyl]-4,4-
difluoropyrrolidine-1-carboxylic acid tert-butyl ester 869527-50-4P,

2- (R) - [2- (S) -Amino-1- (S) -hydroxy-3-phenylpropyl] -4- (R) -fluoropyrrolidine-1-carboxylic acid tert-butyl ester 869527-51-5P, 4- (R) -Fluoro-2- (R) -hydroxymethylpyrrolidine-1-carboxylic acid tert-butyl ester 869527-52-6P, 2- (R) - [2- (S) -Benzyl-1- (S) -hydroxy-3- (4- (S) -isopropyl-2-oxooxazolidin-3-yl) -3-oxopropyl] -4- (R) -fluoropyrrolidine-1-carboxylic acid tert-butyl ester 869527-53-7P, 2- (R) - [2- (S) -Benzyl-1- (S) - [(tert-butyl)dimethylsilyl]oxy] -3- (4- (S) -isopropyl-2-oxooxazolidin-3-yl) -3-oxopropyl] -4- (R) -fluoropyrrolidine-1-carboxylic acid tert-butyl ester 869527-54-8P, 2- (R) - [2- (S) -Azidocarbonyl-1- (S) - [(tert-butyl)dimethylsilyl]oxy] -3-phenylpropyl] -4- (R) -fluoropyrrolidine-1-carboxylic acid tert-butyl ester 869527-55-9P 869527-56-0P, 2- (R) - [2- (R) -Dibenzylamino-1- (S) -hydroxy-3-phenylpropyl]pyrrolidine-1-carboxylic acid tert-butyl ester 869527-57-1P, 2- (S) - [2- (S) -Amino-1- (S) -hydroxy-3-phenylpropyl] -3- (S) -fluoropyrrolidine-1-carboxylic acid tert-butyl ester 869527-58-2P, 2- (S) - [2- (S) -Amino-1- (S) -hydroxy-3-phenylpropyl] -3,3-difluoropyrrolidine-1-carboxylic acid tert-butyl ester 869527-59-3P, 5- [2- (S) -Dibenzylamino-1- (S) -hydroxy-3-phenylpropyl] -4-fluoro-2,3-dihydropyrrole-1-carboxylic acid tert-butyl ester 869527-60-6P, 2- (S) - [2- (S) -Dibenzylamino-1- (S) -hydroxy-3-phenylpropyl] -3,3-difluoropyrrolidine-1-carboxylic acid tert-butyl ester 869527-61-7P, 2- (2R) - [(1S,2S) -2-Acetyl-amino-3- (3,5-difluorophenyl) -1-hydroxypropyl]piperidine-1-carboxylic acid tert-butyl ester 869527-63-9P, 2- (R) - [(1S,2S) -2-Acetyl-amino-3- (3,5-difluorophenyl) -1-hydroxypropyl]pyrrolidine-1-carboxylic acid tert-butyl ester 869527-64-0P, (+) -2- [(1S) -1-Methylpropyl]amino] -6- [(methanesulfonyl) (methyl)amino]isonicotinate potassium salt 869527-65-1P, 2- [(1S) -1-Methylpropyl]amino] -6-chloroisonicotinic acid methyl ester 869527-66-2P, (+) -2- [(1S) -1-Methylpropyl]amino] -6- [(methylsulfonyl)amino]isonicotinic acid methyl ester 869527-67-3P, (+) -2- [(1S) -1-Methylpropyl]amino] -6- [(methylsulfonyl) (methyl)amino]isonicotinic acid methyl ester 869527-68-4P, (2R,4R) -2- [(1S,2S) -2-Amino-3- (3,5-difluorophenyl) -1-hydroxypropyl] -4- (3-methoxyphenoxy)pyrrolidine-1-carboxylic acid tert-butyl ester 869527-69-5P, (2R,4R) -4- (3-Methoxyphenoxy)pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester 869527-70-8P, (2R,4R) -2-Hydroxymethyl-4- (3-methoxyphenoxy)pyrrolidine-1-carboxylic acid tert-butyl ester 869527-71-9P, (2R,4R) -2- [(1R,2S) -3- (3,5-Difluorophenyl) -1-hydroxy-2-nitropropyl] -4- (3-methoxyphenoxy)pyrrolidine-1-carboxylic acid tert-butyl ester 869527-72-0P, (2R,5S) -2- [(1S,2S) -2-Amino-3- (3,5-difluorophenyl) -1-hydroxypropyl] -5-phenylpyrrolidine-1-carboxylic acid tert-butyl ester 869527-73-1P, (2R,5S) -2-Hydroxymethyl-5-phenylpyrrolidine-1-carboxylic acid tert-butyl ester 869527-74-2P, (2R,4R) -2- [(1S,2S) -2-Amino-3- (3,5-difluorophenyl) -1-hydroxypropyl] -4- [(4-methoxybenzyl)oxy]pyrrolidine-1-carboxylic acid tert-butyl ester 869527-75-3P, (2R,4R) -4- [(4-Methoxybenzyl)oxy]pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester 869527-76-4P, 2- (S) - [2- (R) -Amino-1- (S) -hydroxy-3-phenylpropyl]pyrrolidine-1-carboxylic acid tert-butyl ester 869527-77-5P, 2- (S) - [2- (Dibenzylamino) - (1S) -1-hydroxy-3-phenylpropyl]pyrrolidine-1-carboxylic acid tert-butyl ester 869527-78-6P, 2- (S) - [2- (R) -Dibenzylamino-1- (1S) -hydroxy-3-phenylpropyl]pyrrolidine-1-carboxylic acid tert-butyl ester 869527-79-7P, 2- (R) - [2- (S) -Amino-1- (S) -hydroxy-3-phenylpropyl] -5,5-dimethylpyrrolidine-1-carboxylic acid tert-butyl ester 869527-80-0P, 2,2-Dimethylpyrrolidine-1-carboxylic acid tert-butyl ester 869527-81-1P, 2- (R) - [2- (S) -Dibenzylamino-1- (S) -hydroxy-3-phenylpropyl] -5,5-dimethylpyrrolidine-1-carboxylic acid tert-butyl ester 869527-82-2P, (2R,4R) -4-Benzyloxy-2-hydroxymethylpyrrolidine-1-carboxylic acid tert-butyl ester 869527-83-3P, (2R,4R) -4-Benzyloxy-2- [(1R,2S) -3- (3,5-difluorophenyl) -1-hydroxy-2-nitropropyl]pyrrolidine-1-carboxylic acid tert-butyl ester 869527-84-4P, (2R) -2- [(4S,5S) -3-Acetyl-4- (3,5-difluorobenzyl) -2,2-dimethyloxazolidin-5-yl] -4- (carboxymethyl)pyrrolidine-

1-carboxylic acid tert-butyl ester 869527-85-5P, (2R,4R)-2-[(4S,5S)-3-Acetyl-4-(3,5-difluorobenzyl)-2,2-dimethyloxazolidin-5-yl]-4-benzyloxypyrrolidine-1-carboxylic acid tert-butyl ester 869527-87-7P, (2R,4R)-2-[(4S,5S)-3-Acetyl-4-(3,5-difluorobenzyl)-2,2-dimethyloxazolidin-5-yl]-4-hydroxypyrrolidine-1-carboxylic acid tert-butyl ester 869527-88-8P, (2R)-2-[(4S,5S)-3-Acetyl-4-(3,5-difluorobenzyl)-2,2-dimethyloxazolidin-5-yl]-4-oxopyrrolidine-1-carboxylic acid tert-butyl ester 869527-90-2P, (2R)-2-[(4S,5S)-3-Acetyl-4-(3,5-difluorobenzyl)-2,2-dimethyloxazolidin-5-yl]-4-[(methoxycarbonyl)methyl]pyrrolidine-1-carboxylic acid tert-butyl ester 869527-91-3P, 1-(3,5-Difluorophenyl)-2-nitroethane 869527-92-4P, 1-(3,5-Difluorophenyl)-2-nitroethanol 869527-93-5P, 2-[[[(1S)-1-Methylpropyl]amino]-6-[(cyclopropylsulfanyl)(methyl)amino]isonicotinic acid 869527-94-6P, 2-[[[(1S)-1-Methylpropyl]amino]-6-[(cyclopropylsulfonyl)(methyl)amino]isonicotinic acid methyl ester 869527-95-7P, 2-[[[(1S)-1-Methylpropyl]amino]-6-[(cyclopropyl)(methylsulfonyl)amino]isonicotinic acid 869527-96-8P, 2-[[[(1S)-1-Methylpropyl]amino]-6-[[[propan-2-yl)sulfonyl]amino]isonicotinic acid 869527-97-9P, 2-[[[(1S)-1-Methylpropyl]amino]-6-[methyl[(propan-2-yl)sulfonyl]amino]isonicotinic acid 869527-98-0P, 2-[[[(1S)-1-Methylpropyl]amino]-6-[ethyl(methylsulfonyl)amino]isonicotinic acid 869527-99-1P, 2-[[[(1S)-1-Methylpropyl]amino]-6-[(2-fluoroethyl)(methylsulfonyl)amino]isonicotinic acid 869528-00-7P, 2-[[[(1S)-1-Methylpropyl]amino]-6-[(2,2-difluoroethyl)(methylsulfonyl)amino]isonicotinic acid 869528-01-8P, 2-[[[(1S)-1-Methylpropyl]amino]-6-[(2,2,2-trifluoroethyl)(methylsulfonyl)amino]isonicotinic acid 869528-02-9P, 2-[[[(1S)-1-Methylpropyl]amino]-6-([1,3]dioxan-2-yl)isonicotinic acid 869528-03-0P, 2-Chloro-6-([1,3]dioxan-2-yl)isonicotinic acid methyl ester 869528-04-1P, 2-Chloro-6-([1,3]dioxan-2-yl)isonicotinic acid methyl ester 869528-05-2P, 2-[[[(1S)-1-Methylpropyl]amino]-6-([1,3]dioxan-2-yl)isonicotinic acid methyl ester 869528-06-3P, 2-[[[(1S)-1-Methylpropyl]amino]-6-([1,3]dioxolan-2-yl)isonicotinic acid 869528-07-4P, 2-Chloro-6-difluoromethylisonicotinic acid methyl ester 869528-08-5P, 2-[[[(1S)-1-Methylpropyl]amino]-6-difluoromethylisonicotinic acid methyl ester 869528-09-6P, 2-[[[(1S)-1-Methylpropyl]amino]-6-(1,1-difluoroethyl)isonicotinic acid 869528-10-9P, 2-Acetyl-6-chloroisonicotinic acid methyl ester 869528-11-0P, 2-Chloro-6-(1,1-difluoroethyl)isonicotinic acid methyl ester 869528-12-1P, 2-[[[(1S)-1-Methylpropyl]amino]-6-(1,1-difluoroethyl)isonicotinic acid methyl ester 869528-13-2P, 2-[[[(1S)-1-Methylpropyl]amino]-6-(2-oxopropyl)isonicotinic acid 869528-14-3P, 2-Chloro-6-(2-oxopropyl)isonicotinic acid methyl ester 869528-15-4P, 2-[[[(1S)-1-Methylpropyl]amino]-6-(2-oxopropyl)isonicotinic acid methyl ester 869528-16-5P, 2-Chloro-6-(2,2-difluoropropyl)isonicotinic acid methyl ester 869528-17-6P, 2-[[[(1S)-1-Methylpropyl]amino]-6-(2,2-difluoropropyl)isonicotinic acid methyl ester 869528-18-7P, 2-Acetyl-6-[[[(1S)-1-methylpropyl]amino]isonicotinic acid 869528-19-8P, 2-Acetyl-6-[[[(1S)-1-methylpropyl]amino]isonicotinic acid methyl ester 869528-20-1P, 6-[[[(1S)-1-Methylpropyl]amino]pyridine-2,4-dicarboxylic acid 2-ethyl ester 4-methyl ester 869528-21-2P, 6-Methoxypyridine-2,4-dicarboxylic acid 2-ethyl ester 4-methyl ester 869528-22-3P, 2-[[[(1S)-1-Methylpropyl]amino]-6-cyanoisonicotinic acid 869528-23-4P, (S)-2-sec-Butylamino-6-cyanoisonicotinic acid methyl ester 869528-24-5P, 2-[[[(1S)-1-Methylpropyl]amino]-6-methylsulfonylisonicotinic acid 869528-25-6P, 2-[[[(1S)-1-Methylpropyl]amino]-6-methylsulfonylisonicotinic acid methyl ester 869528-26-7P, 2-[[[(1S)-1-Methylpropyl]amino]-6-methylsulfonylisonicotinic acid methyl ester 869528-27-8P, 2-[[[(1S)-1-Methylpropyl]amino]-6-propylsulfonylisonicotinic acid 869528-28-9P, 2-Chloro-6-propylsulfonylisonicotinic acid methyl ester 869528-29-0P, 2-Chloro-6-propylsulfonylisonicotinic acid methyl ester 869528-30-3P, 2-[[[(1S)-1-Methylpropyl]amino]-6-propylsulfonylisonicotinic

acid methyl ester 869528-31-4P, 2-(((1S)-1-Methylpropyl)amino]-6-isopropylsulfonylisonicotinic acid 869528-32-5P, 2-Chloro-6-isopropylsulfonylisonicotinic acid methyl ester 869528-33-6P, 2-(((1S)-1-Methylpropyl)amino]-6-isopropylsulfonylisonicotinic acid methyl ester 869528-34-7P, 2-(((1S)-1-Methylpropyl)amino]-6-(cyclopropylsulfonyl)isonicotinic acid 869528-35-8P, 2-(((1S)-1-Methylpropyl)amino]-6-(cyclopentylsulfonyl)isonicotinic acid 869528-36-9P, 2-((Propan-2-yl)sulfonyl)-6-((prop-2-ynyl)amino)isonicotinic acid 869528-37-0P, 2-((Propan-2-yl)sulfonyl)-6-((prop-2-ynyl)amino)isonicotinic acid methyl ester 869528-38-1P, 2-Cyclopropylamino-6-isopropylsulfonylisonicotinic acid 869528-39-2P, 2-((Cyclopropyl)(methyl)amino)-6-isopropylsulfonylisonicotinic acid 869528-40-5P, 2-Cyclobutylamino-6-isopropylsulfonylisonicotinic acid 869528-41-6P, 2-Cyclopropylamino-6-(cyclopropylsulfonyl)isonicotinic acid 869528-42-7P, 2-Chloro-6-(cyclopropylsulfonyl)isonicotinic acid tert-butyl ester 869528-43-8P, 2-Cyclopropylamino-6-(cyclopropylsulfonyl)isonicotinic acid tert-butyl ester 869528-44-9P, 2-(((1S)-1-Methylpropyl)amino)-6-((methylsulfonyl)(methyl)amino)isonicotinic acid 869528-45-0P, 2-(((1S)-1-Methylpropyl)amino)-6-((methylsulfonyl)amino)isonicotinic acid 869528-46-1P, 2-(((1S)-1-Methylpropyl)amino)-6-(1,1-dioxo-[1,2]thiazinan-2-yl)isonicotinic acid 869528-47-2P, 2-(((1S)-1-Methylpropyl)amino)-6-(1,1-dioxo-[1,2]thiazinan-2-yl)isonicotinic acid methyl ester 869528-48-3P, 2-(((1S)-1-Methylpropyl)amino)-6-(1,1-dioxoisothiazolidin-2-yl)isonicotinic acid 869528-49-4P, 2-(((1S)-1-Methylpropyl)amino)-6-dimethylsulfamoylisonicotinic acid 869528-50-7P, 2-Benzylsulfanyl-6-chloroisonicotinic acid methyl ester 869528-51-8P, 2-(((1S)-1-Methylpropyl)amino)-6-dimethylsulfamoylisonicotinic acid methyl ester 869528-52-9P, 2-(((1S)-1-Methylpropyl)amino)-6-methylsulfamoylisonicotinic acid 869528-53-0P, 2-(((1S)-1-Methylpropyl)amino)-6-((pyrrolidin-1-yl)sulfonyl)isonicotinic acid 869528-54-1P, 6-(Cyclobutylamino)pyridine-2,4-dicarboxylic acid 2-ethyl ester 869528-55-2P, 6-(Cyclobutylamino)pyridine-2,4-dicarboxylic acid 2-ethyl ester 4-methyl ester 869528-56-3P, 2-(((1S)-1-Methylpropyl)amino)-6-((propan-1-yl)sulfinyl)isonicotinic acid 869528-57-4P, 2-(((1S)-1-Methylpropyl)amino)-6-propylsulfanylisonicotinic acid methyl ester 869528-58-5P, 2-(((1S)-1-Methylpropyl)amino)-6-((propan-1-yl)sulfinyl)isonicotinic acid methyl ester 869528-59-6P, 2-(((1S)-1-Methylpropyl)amino)-6-((methan-1-yl)sulfinyl)isonicotinic acid 869528-60-9P, 2-(((1S)-1-Methylpropyl)amino)-6-(2-fluorophenyl)isonicotinic acid 869528-61-0P, 2-(((1S)-1-Methylpropyl)amino)-6-(2-fluorophenyl)isonicotinic acid methyl ester 869528-62-1P, 2-Cyclopropylamino-6-((methylsulfonyl)(methyl)amino)isonicotinic acid 869528-63-2P, 2-Chloro-6-((methylsulfonyl)amino)isonicotinic acid methyl ester 869528-64-3P, 2-Cyclopropylamino-6-((methylsulfonyl)(methyl)amino)isonicotinic acid methyl ester 869528-65-4P, 2-(((1S)-1-Methylpropyl)amino)-6-(2H-tetrazol-5-yl)isonicotinic acid 869528-66-5P, 2-(((1S)-1-Methylpropyl)amino)-6-(2H-tetrazol-5-yl)isonicotinic acid methyl ester 869528-67-6P, 2-(((1S)-1-Methylpropyl)amino)-6-(2-ethyl-2H-tetrazol-5-yl)isonicotinic acid 869528-68-7P, 2-(((1S)-1-Methylpropyl)amino)-6-(1-ethyl-1H-tetrazol-5-yl)isonicotinic acid 869528-69-8P, 2-(((1S)-1-Methylpropyl)amino)-6-(2-ethyl-2H-tetrazol-5-yl)isonicotinic acid methyl ester 869528-70-1P, 2-(((1S)-1-Methylpropyl)amino)-6-(1-ethyl-1H-tetrazol-5-yl)isonicotinic acid methyl ester 869528-71-2P, 2-(((1S)-1-Methylpropyl)amino)-6-(2-methyl-2H-tetrazol-5-yl)isonicotinic acid 869528-72-3P, 2-(((1S)-1-Methylpropyl)amino)-6-(2-methyl-2H-tetrazol-5-yl)isonicotinic acid methyl ester 869528-73-4P, 2-(((1S)-1-Methylpropyl)amino)isonicotinic acid 869528-74-5P, 2-(((1S)-1-Methylpropyl)amino)-6-difluoromethoxyisonicotinic acid 869528-75-6P, 2-(((1S)-1-Methylpropyl)amino)-6-methoxyisonicotinic acid ethyl ester 869528-76-7P,

2-(((1S)-1-Methylpropyl)amino)-6-hydroxyisonicotinic acid ethyl ester 869528-77-8P, 2-(((1S)-1-Methylpropyl)amino)-6-difluoromethoxyisonicotinic acid ethyl ester 869528-78-9P, 2-Methylsulfonyl-6-(methylpropylamino)isonicotinic acid 869528-79-0P, 2-Chloro-6-methylsulfonylisonicotinic acid methyl ester 869528-80-3P, 2-Methylsulfonyl-6-[(methyl)(propyl)amino]isonicotinic acid methyl ester 869528-81-4P, 2-Cyclobutylamino-6-methylsulfonylisonicotinic acid 869528-82-5P, 2-Cyclobutylamino-6-methylsulfonylisonicotinic acid methyl ester 869528-83-6P, 2-(Pyrrolidin-1-yl)-6-methylsulfonylisonicotinic acid 869528-84-7P, 2-[(Methylsulfonyl)(methyl)amino]-6-(methylpropylamino)isonicotinic acid 869528-85-8P, 2-Chloro-6-[(methyl)(propyl)amino]isonicotinic acid methyl ester 869528-86-9P, 2-[(Methylsulfonyl)amino]-6-[(methyl)(propyl)amino]isonicotinic acid methyl ester 869528-87-0P, 2-[(Methylsulfonyl)(methyl)amino]-6-(methylpropylamino)isonicotinic acid methyl ester 869528-88-1P, 2-Phenylsulfonyl-6-(((1S)-1-methylpropyl)amino)isonicotinic acid 869528-89-2P, 2-Phenylsulfonyl-6-chloroisonicotinic acid methyl ester 869528-90-5P 869528-91-6P, 2-[(1-Methylpropyl)amino]-6-[(methylsulfonyl)oxy]isonicotinic acid 869528-92-7P, 2-Benzoyloxy-6-[(1-methylpropyl)amino]isonicotinic acid methyl ester 869528-93-8P, 2-[(1-Methylpropyl)amino]-6-hydroxyisonicotinic acid 869528-94-9P, 2-[(1-Methylpropyl)amino]-6-[(methylsulfonyl)oxy]isonicotinic acid methyl ester 869528-95-0P, 6-Fluoro-N,N-dipropylisophthalamide acid 869528-96-1P, 3-Bromo-4-fluoro-N,N-dipropylbenzamide 869528-97-2P, 3-Cyano-4-fluoro-N,N-dipropylbenzamide 869528-98-3P, 5-(N-Methyl-N-propylcarbamoyl)isophthalic acid monoethyl ester 869528-99-4P, Diethyl 5-(N-Methyl-N-propylcarbamoyl)isophthalate 869529-00-0P, 3-Ethylcarbamoyl-5-(N-methyl-N-propylcarbamoyl)benzoic acid 869529-01-1P, 3-Ethylcarbamoyl-5-(N-methyl-N-propylcarbamoyl)benzoic acid ethyl ester 869529-02-2P, 3,5-Bis[(methyl)(propyl)carbamoyl]benzoic acid 869529-03-3P, 3,5-Bis[(methyl)(propyl)carbamoyl]benzoic acid ethyl ester 869529-04-4P, 5-(N-Methyl-N-propylcarbamoyl)isophthalic acid monoisopropyl ester 869529-05-5P

, 5-(N-Methyl-N-propylcarbamoyl)isophthalic acid 1-ethyl ester 3-isopropyl ester 869529-06-6P, 5-Difluoromethyl-N-methyl-N-propylisophthalamide acid 869529-07-7P, 5-Hydroxymethyl-N-methyl-N-propylisophthalamide acid ethyl ester 869529-08-8P, 5-Formyl-N-methyl-N-propylisophthalamide acid ethyl ester 869529-09-9P, 5-Difluoromethyl-N-methyl-N-propylisophthalamide acid ethyl ester 869529-10-2P, 5-Fluoromethyl-N-methyl-N-propylisophthalamide acid 869529-11-3P, 5-Fluoromethyl-N-methyl-N-propylisophthalamide acid ethyl ester 869529-12-4P, N-Methyl-N-propyl-5-vinylisophthalamide acid 869529-13-5P, 5-Bromo-N-methyl-N-propylisophthalamide acid methyl ester 869529-14-6P, N-Methyl-N-propyl-5-vinylisophthalamide acid methyl ester 869529-15-7P, N-Methyl-5-(oxazol-2-yl)-N-propylisophthalamide acid methyl ester 869529-16-8P, N-Methyl-5-(3-methyl-[1,2,4]oxadiazol-5-yl)-N-propylisophthalamide acid 869529-17-9P, N-Methyl-5-(3-methyl-[1,2,4]oxadiazol-5-yl)-N-propylisophthalamide acid ethyl ester 869529-18-0P, N-Methyl-5-(oxazol-5-yl)-N-propylisophthalamide acid 869529-19-1P, 5-(2,2-Difluorovinyl)-N-methyl-N-propylisophthalamide acid 869529-20-4P, 5-(2,2-Difluorovinyl)-N-methyl-N-propylisophthalamide acid ethyl ester 869529-21-5P, N-Methyl-5-[(2-methylpyrrolidin-1-yl)carbonyl]-N-propylisophthalamide acid 869529-22-6P, N-Methyl-5-[(2-methylpyrrolidin-1-yl)carbonyl]-N-propylisophthalamide acid ethyl ester 869529-23-7P, 5-[(3,3-Difluoropyrrolidin-1-yl)carbonyl]-N-methyl-N-propylisophthalamide acid 869529-24-8P, 5-[(3,3-Difluoropyrrolidin-1-yl)carbonyl]-N-methyl-N-propylisophthalamide acid ethyl ester 869529-25-9P, 5-Chloro-N-methyl-N-propylisophthalamide acid 869529-26-0P, N-Methyl-5-propoxy-N-propylisophthalamide acid 869529-27-1P, 5-Propoxyisophthalic acid monomethyl ester 869529-28-2P, 5-Methylsulfonyl-N-methyl-N-propylisophthalamide acid 869529-29-3P, Dimethyl 5-

methylsulfonylisophthalate 869529-30-6P 869529-31-7P,
 5-Dimethylsulfamoylisophthalic acid monomethyl ester 869529-32-8P,
 N-Methyl-5-(2-methylprop-1-enyl)-N-propylisophthalamide
 869529-33-9P, Diethyl 5-(2-methylprop-1-enyl)isophthalate 869529-34-0P,
 6-Fluoro-5-methylsulfonyl-N-methyl-N-propylisophthalamide
 869529-35-1P, 3-Bromo-5-chlorosulfonyl-4-fluorobenzoic acid
 869529-36-2P, 3-Bromo-4-fluoro-5-methylsulfonylbenzoic acid
 869529-37-3P, 3-Bromo-4-fluoro-5-methylsulfonyl-N-methyl-N-propylbenzamide
 869529-38-4P, 5-[(Methylsulfonyl)(methyl)amino]-N-methyl-N-propylisophthalamide
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(intermediate; preparation of amides as BACE inhibitors for treating
 Alzheimer's)

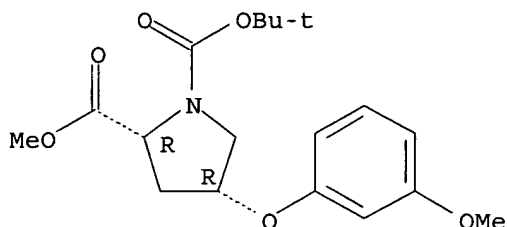
IT 869527-69-5P, (2R,4R)-4-(3-Methoxyphenoxy)pyrrolidine-1,2-
 dicarboxylic acid 1-tert-butyl ester 2-methyl ester
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(intermediate; preparation of amides as BACE inhibitors for treating
 Alzheimer's)

RN 869527-69-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(3-methoxyphenoxy)-,
 1-(1,1-dimethylethyl) 2-methyl ester, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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 the sweet taste chemoreception mechanism

AUTHOR(S): Bassoli, Angela; Borgonovo, Gigliola; Busnelli,
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CORPORATE SOURCE: Dipartimento di Scienze Molecolari Agroalimentari -
 DISMA, Sezione di Chimica, Università di Milano,
 Milan, 20133, Italy

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AB The sweet natural compound monatin 1 has two stereogenic centers, and the
 2S,4S absolute configuration has been attributed previously to the natural
 isomer. Among the four stereoisomers of monatin, three of them,
 particularly the 2R,4R isomer, tastes intensely sweet. The conformations
 of the four compds. have been studied by means of mol. modeling
 techniques. Both the diastereoisomeric forms show strong intramol.
 hydrogen bonds which involve different functional groups and give rise to

two different min. energy conformations. The tertiary alc. group in monatin seems to be indirectly involved in the generation of the taste, acting as an important constraint in generating the active conformation. The most important glucophores have been identified in the terminal -NH₃⁺ and -COO⁻ groups and in the indole ring by comparison with known topol. models of sweet compds. and through the synthesis of appropriate derivs. in which some of these groups are lacking or modified. The relative affinity of each stereoisomer for its putative sweet taste receptor has been estimated semi-quant. with the pseudoreceptor modeling technique. The predicted activity calculated with this technique is in good agreement with the exptl. data and explains why the 2R,4R isomer (and not the natural 2S,4S isomer) is the sweetest of the series.

CC 17-6 (Food and Feed Chemistry)

Section cross-reference(s): 13, 27

IT 58550-81-5P 108963-96-8P 612820-01-6P **862583-27-5P**

862583-29-7P 862583-32-2P 862583-35-5P 862583-36-6P 862583-37-7P
862583-38-8P

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(modeling sweet taste chemoreception mechanism of monatin, its stereoisomers and derivs.)

IT **862583-27-5P**

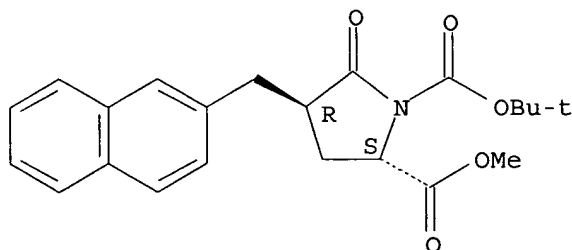
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(modeling sweet taste chemoreception mechanism of monatin, its stereoisomers and derivs.)

RN 862583-27-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenylmethyl)-5-oxo-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 3 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:300434 CAPLUS

DOCUMENT NUMBER: 142:374111

TITLE: Preparation of proline quinazoline derivatives as antiproliferative agents

INVENTOR(S): Bradbury, Robert Hugh; Halsall, Christopher Thomas; Hennequin, Laurent Francois Andre; Kettle, Jason Grant; Plowright, Allyn

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Ltd.

SOURCE: PCT Int. Appl., 198 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030757	A1	20050407	WO 2004-GB4085	20040922
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

GB 2003-22409

A 20030925

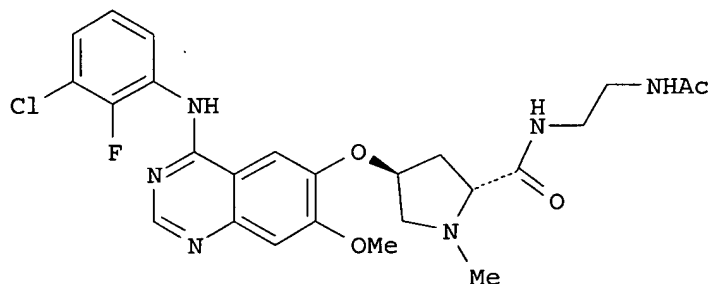
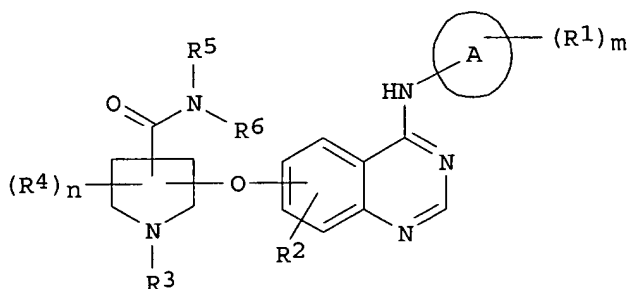
GB 2003-22534

A 20030926

OTHER SOURCE(S):

MARPAT 142:374111

GI



AB The invention relates to quinazoline derivs. I [R2 or the substituted pyrrolidinyloxy group is in the 6 or 7 position of the quinazoline ring; A is Ph or pyridyl; m is 0-3; n is 0-2; R1 is halo, cyano, nitro, hydroxy, carboxy, trifluoromethyl, alkyl, alkoxy, alkylsulfonyl, alkylureido, etc.; R2 is H, alkyl, cycloalkyl, cycloalkylalkyl or (un)substituted alkoxy; R3 is H, alkyl, cycloalkyl, alkylthio, alkylsulfinyl, carbamoylalkyl, etc.; R4 is alkyl, alkoxy, cyano, halo, hydroxy or oxo; R5 is H or alkyl; R6 is H, alkyl, alkoxy, heterocyclyl, heteroaryl, etc.; or R5R6N is a ring], including processes for their preparation, pharmaceutical compns. containing them,

and their use as antiproliferative agents in the prevention or treatment

of tumors which are sensitive to inhibition of erbB receptor tyrosine kinases. Thus, compound II was prepared by etherification of Boc-protected cis-4-hydroxy-D-proline Me ester with 4-chloro-7-methoxyquinazolin-6-ol and reaction of the product with 3-chloro-2-fluoroaniline in 4.0 M HCl/dioxane and acetonitrile, followed by reductive N-methylation, saponification, and amidation. Compound II showed IC₅₀ = 0.008 nM for inhibition of EGFR tyrosine kinase protein phosphorylation and IC₅₀ = 0.144 nM in the EGFR driven KB cell proliferation assay.

IC ICM C07D403-12
ICS C07D403-14; C07D401-14; C07D405-14; C07D409-14; C07D413-14; A61K031-517; A61P035-00

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 28, 63

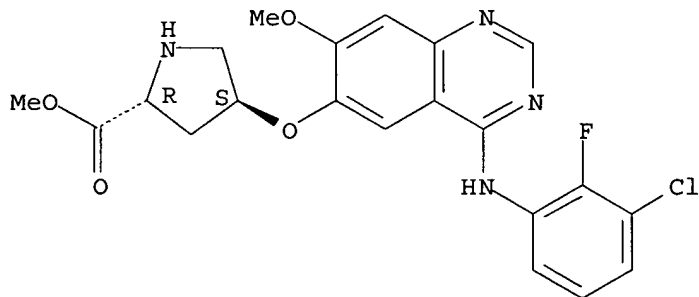
IT 16064-25-8P 114676-69-6P 127423-55-6P 574745-97-4P
849344-98-5P 849344-99-6P 849345-00-2P
849345-09-1P 849345-11-5P 849345-12-6P 849345-13-7P 849345-14-8P
849345-15-9P 849345-17-1P 849345-18-2P 849345-19-3P
849345-40-0P 849345-41-1P 849345-42-2P 849345-43-3P
849345-44-4P 849345-45-5P 849345-89-7P
849345-90-0P 849345-91-1P 849345-92-2P
849346-14-1P 849346-15-2P 849346-16-3P
849346-17-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of proline quinazoline derivs. as antiproliferative agents)

IT 849344-98-5P 849344-99-6P 849345-00-2P
849345-40-0P 849345-43-3P 849345-44-4P
849345-45-5P 849345-89-7P 849345-90-0P
849345-91-1P 849345-92-2P 849346-14-1P
849346-15-2P 849346-16-3P 849346-17-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of proline quinazoline derivs. as antiproliferative agents)

RN 849344-98-5 CAPLUS

CN D-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

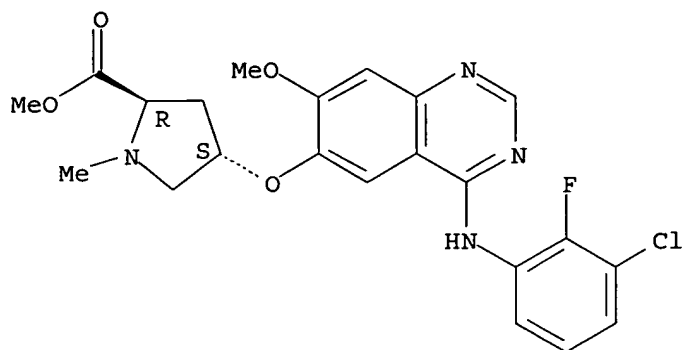
Absolute stereochemistry.



RN 849344-99-6 CAPLUS

CN D-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

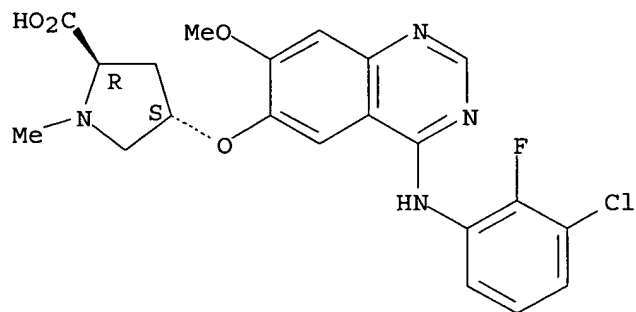
Absolute stereochemistry.



RN 849345-00-2 CAPLUS

CN D-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, (4S)- (9CI) (CA INDEX NAME)

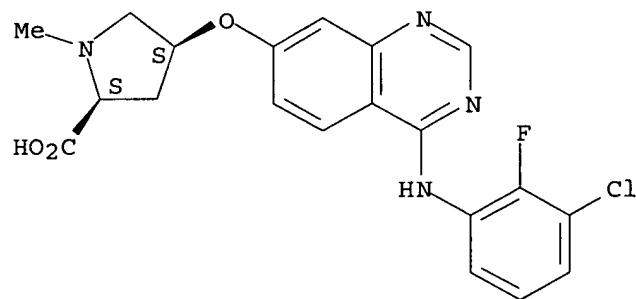
Absolute stereochemistry.



RN 849345-40-0 CAPLUS

CN L-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-quinazolinyl]oxy]-1-methyl-, (4S)- (9CI) (CA INDEX NAME)

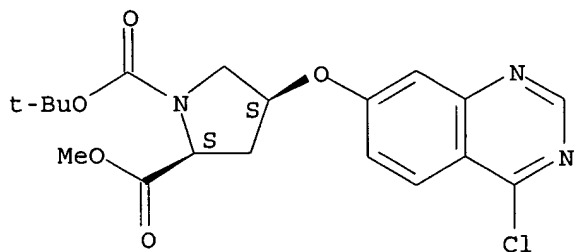
Absolute stereochemistry.



RN 849345-43-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(4-chloro-7-quinazolinyl)oxy]-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

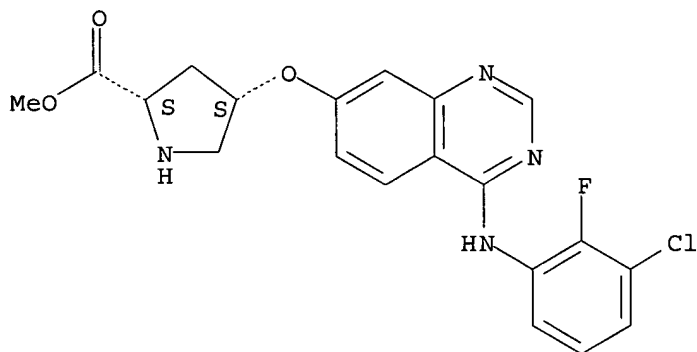
Absolute stereochemistry.



RN 849345-44-4 CAPLUS

CN L-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-quinazolinyl]oxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

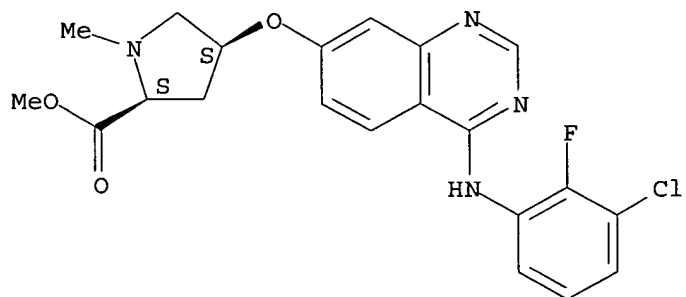
Absolute stereochemistry.



RN 849345-45-5 CAPLUS

CN L-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-quinazolinyl]oxy]-1-methyl-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

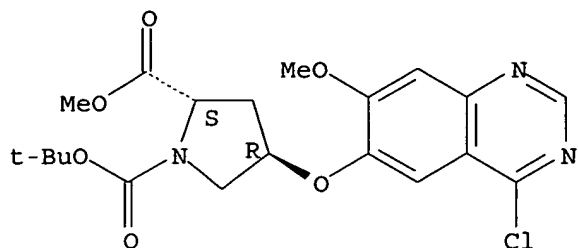
Absolute stereochemistry.



RN 849345-89-7 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(4-chloro-7-methoxy-6-quinazolinyl)oxy]-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

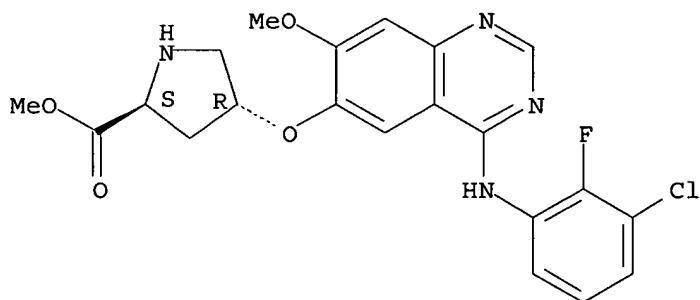
Absolute stereochemistry.



RN 849345-90-0 CAPLUS

CN L-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-, methyl ester, monohydrochloride, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

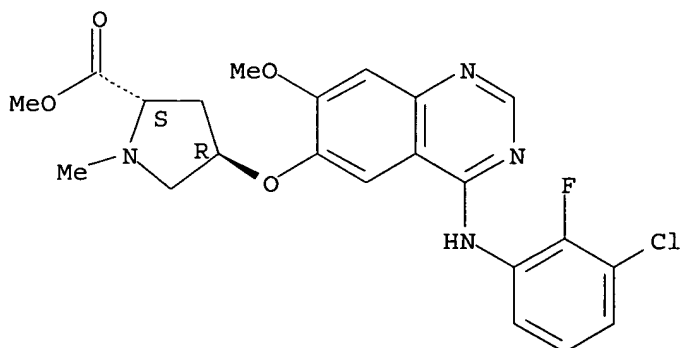


● HCl

RN 849345-91-1 CAPLUS

CN L-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

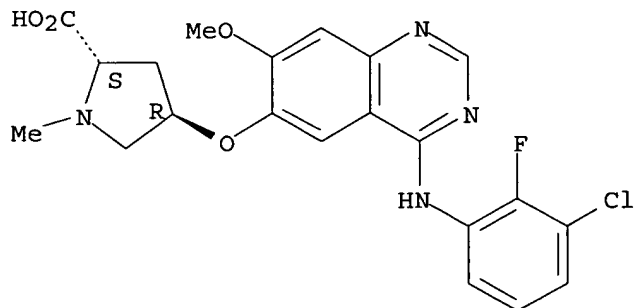
Absolute stereochemistry.



RN 849345-92-2 CAPLUS

CN L-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, (4R)- (9CI) (CA INDEX NAME)

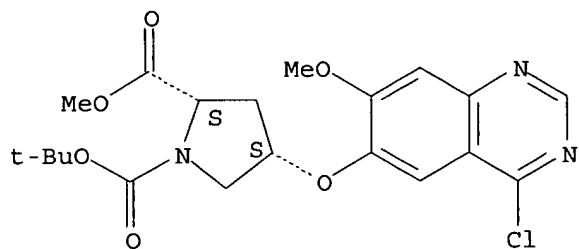
Absolute stereochemistry.



RN 849346-14-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(4-chloro-7-methoxy-6-quinazolinyl)oxy]-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

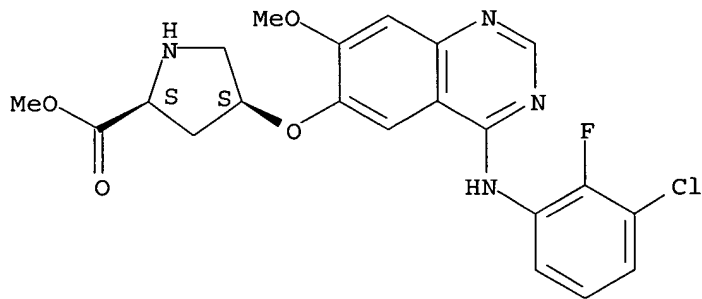
Absolute stereochemistry.



RN 849346-15-2 CAPLUS

CN L-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

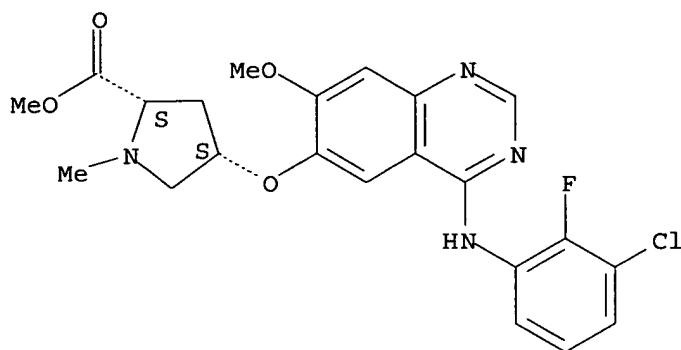
Absolute stereochemistry.



RN 849346-16-3 CAPLUS

CN L-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

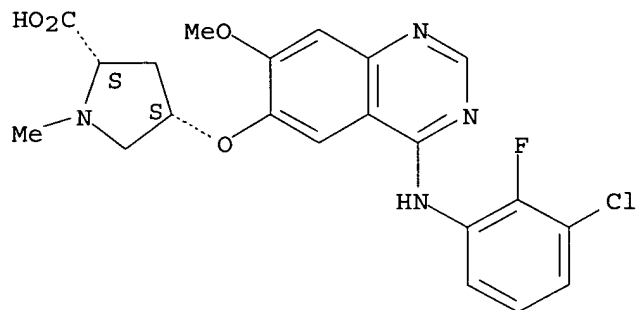
Absolute stereochemistry.



RN 849346-17-4 CAPLUS

CN L-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 4 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1067791 CAPLUS

DOCUMENT NUMBER: 142:198338

TITLE: The Effects of Conformational Constraints and Steric Bulk in the Amino Acid Moiety of Philanthotoxins on AMPAR Antagonism

AUTHOR(S): Jorgensen, Malene R.; Olsen, Christian A.; Mellor, Ian R.; Usherwood, Peter N. R.; Witt, Matthias; Franzyk, Henrik; Jaroszewski, Jerzy W.

CORPORATE SOURCE: Department of Medicinal Chemistry, The Danish University of Pharmaceutical Sciences, Copenhagen, DK-2100, Den.

SOURCE: Journal of Medicinal Chemistry (2005) 48(1), 56-70
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Philanthotoxin-343 (PhTX-343), a synthetic analog of wasp toxin PhTX-433, is a noncompetitive antagonist at ionotropic receptors (e.g., AChR or iGluR). To determine possible effects of variations of the amino acid side chain, a library consisting of seventeen PhTX-343 analogs was prepared. Thus, tyrosine was replaced by either apolar, conformationally

constrained, or bulky amino acids, whereas the acyl unit and the polyamine moiety were kept unchanged. Analogs with tertiary amide groups were also prepared. Pentafluorophenyl esters were employed for amide bond formation, establishing general protocols for philanthotoxin solution- and solid-phase synthesis (39-90% and 42-54% overall yields, resp.). The analogs were tested for their ability to antagonize kainate-induced currents of 2-amino-3-(3-hydroxy-5-methyl-4-isoxazolyl)propanoic acid receptors (AMPA) expressed in *Xenopus* oocytes from rat brain mRNA. This showed that steric bulk in the amino acid moiety is well tolerated and suggests that binding to AMPAR does not involve the α -NHCO group as a donor in hydrogen bonding.

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT 1202-04-6P, Methyl 1H-indole-2-carboxylate 59040-84-5P 64187-48-0P
 78348-24-0P 114459-62-0P 132684-59-4P 135944-07-9P 135944-08-0P
 177213-61-5DP, polymer-supported 177213-61-5P 178119-93-2P
 178432-51-4P 188837-56-1P 199110-64-0P 215190-19-5P 264273-07-6P
755707-37-0P 839719-66-3P 839719-67-4P 839719-68-5P
 839719-69-6P 839719-70-9P 839719-71-0P 839719-72-1P 839719-73-2P
 839719-74-3P 839719-75-4P 839719-76-5P 839719-77-6P 839719-79-8P
839719-80-1P 839719-81-2P 839719-82-3P
 839719-84-5P 839720-17-1P 839720-18-2P 839720-19-3P 839720-20-6P
 839720-21-7P 839720-22-8P 839720-23-9P 839720-24-0P 839720-25-1P
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 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (effects of conformational constraints and steric bulk in the amino
 acid moiety of philanthotoxin analogs on AMPAR antagonism)

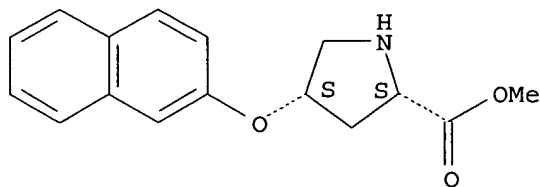
IT **755707-37-0P 839719-80-1P 839719-81-2P**
839719-82-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (effects of conformational constraints and steric bulk in the amino
 acid moiety of philanthotoxin analogs on AMPAR antagonism)

RN 755707-37-0 CAPLUS

CN L-Proline, 4-(2-naphthalenyloxy)-, methyl ester, (4S)- (9CI) (CA INDEX
 NAME)

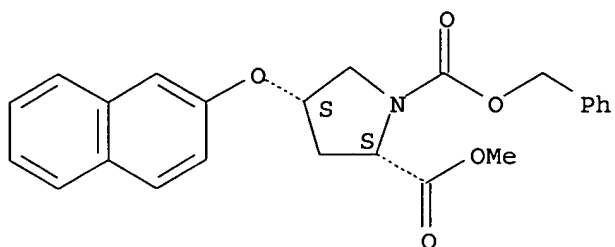
Absolute stereochemistry.



RN 839719-80-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-, 2-methyl
 1-(phenylmethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

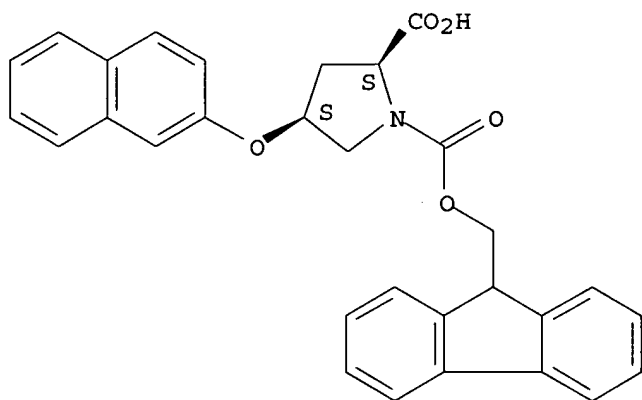
Absolute stereochemistry.



RN 839719-81-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-,
1-(9H-fluoren-9-ylmethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

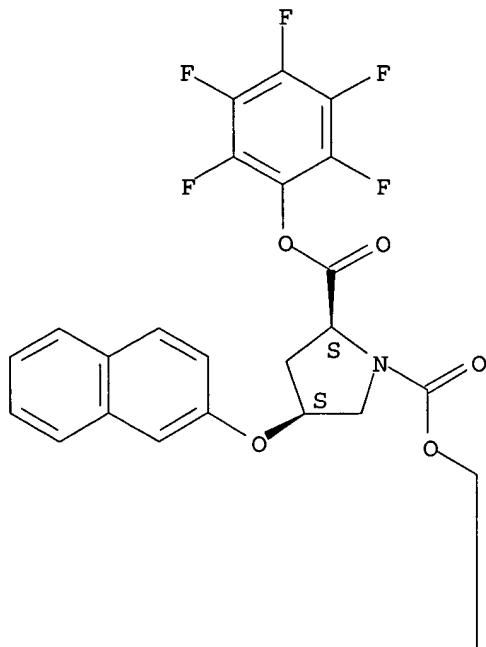


RN 839719-82-3 CAPLUS

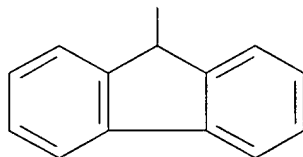
CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-,
1-(9H-fluoren-9-ylmethyl) 2-(pentafluorophenyl) ester, (2S,4S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 5 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:996144 CAPLUS

DOCUMENT NUMBER: 141:410935

TITLE: Preparation of substituted diphenyl isoxazoles, pyrazoles and oxadiazoles for treating HCV infection

INVENTOR(S): Singh, Rajinder; Goff, Dane; Partridge, John

PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 188 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

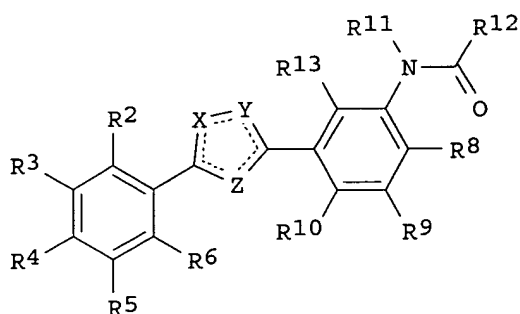
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099164	A1	20041118	WO 2004-US13492 *	20040503

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004266840 A1 20041230 US 2004-838133
 PRIORITY APPLN. INFO.: US 2003-467811P
 OTHER SOURCE(S): MARPAT 141:410935
 GI

20040503
 20030502



I

AB The present invention relates to substituted di-Ph heterocycle compds. I [X, Y = N, O, provided that X and Y are not both O; Z = N, CH, provided that Z = CH when X and Y are both N; R2-R5, R8-R10, R13 = H, OH, SH, CN, etc.; R11 = H, alkyl; R12 = dihalomethyl; R6 = (un)substituted piperazino, piperidino, pyrrolidino, etc.] and pharmaceutical compns. thereof that inhibit replication of HCV virus. E.g., a 3-step synthesis of 2,2-dichloro-N-{3-[3-(2,6-dichlorophenyl)-5-isoxazolyl]phenyl}acetamide, starting from 2,6-dichlorobenzaldoxime, was given. Exemplary compds. I were tested in HCV replicon assay and/or in Western blot assay (biol. data given). The present invention also relates to the use of the compds. and/or compns. (such as liposome suspension) to inhibit HCV replication and/or proliferation and to treat or prevent HCV infections.

IC ICM C07D261-08

ICS C07D271-06; A61K031-42; A61K031-4245

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 63

IT 286841-27-8P	524684-61-5P	524684-62-6P	524684-63-7P	524684-64-8P
524684-65-9P	524684-66-0P	524684-67-1P	524684-68-2P	524684-69-3P
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793708-45-9P	793708-46-0P	793708-47-1P	793708-48-2P	793708-49-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted di-Ph isoxazoles, pyrazoles and oxadiazoles for treating HCV infection)

IT **793707-92-3P 793707-93-4P**

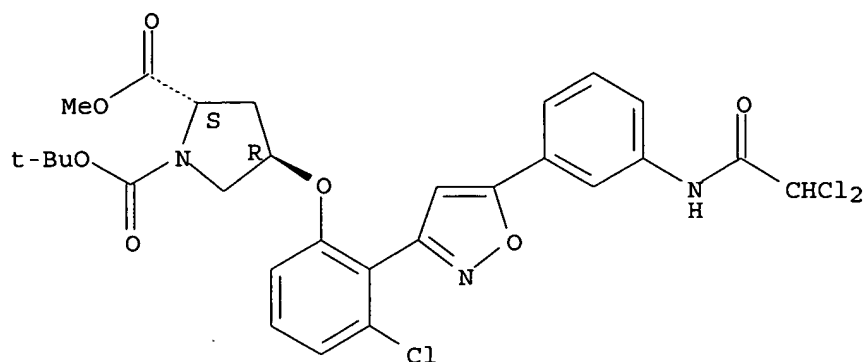
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted di-Ph isoxazoles, pyrazoles and oxadiazoles for treating HCV infection)

RN 793707-92-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[3-chloro-2-[5-[3-
[[dichloroacetyl]amino]phenyl]-3-isoxazolyl]phenoxy]-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

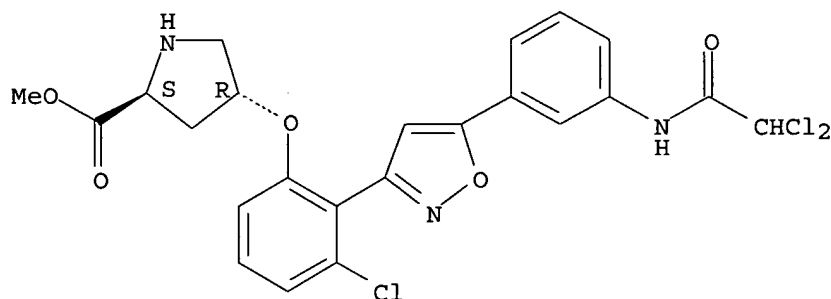
Absolute stereochemistry.



RN 793707-93-4 CAPLUS

CN L-Proline, 4-[3-chloro-2-[5-[3-[(dichloroacetyl)amino]phenyl]-3-isoxazolyl]phenoxy]-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 6 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:927230 CAPLUS

DOCUMENT NUMBER: 141:395807

TITLE: Preparation of macrocyclic isoquinoline peptide inhibitors of hepatitis C virus

INVENTOR(S): McPhee, Fiona; Campbell, Jeffrey Allen; Li, Wenying; D'Andrea, Stanley; Zheng, Zhizhen Barbara; Good, Andrew Charles; Carini, David J.; Johnson, Barry L.; Scola, Paul Michael

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 280 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094452	A2	20041104	WO 2004-US11824	20040416
WO 2004094452	A3	20050519		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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US 2005090432 A1 20050428 US 2004-825693 20040416

EP 1629000 A2 20060301 EP 2004-759941 20040416

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.: US 2003-463423P P 20030416
 WO 2004-US11824 W 20040416

OTHER SOURCE(S): MARPAT 141:395807

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention discloses macrocyclic isoquinoline peptides I [R1-R6 are independently H, alkyl, cycloalkyl, alkoxy, cyano, halo, hydroxy, alkanoyl, nitro, amino, carboxyl, alkylsulfonyl, etc.; R7 is NH2 or NR10R11, where R10 is alkyl, haloalkyl, carbamoyl, carboxy or thiocarboxy ester or an acyl group; R11 is H, alkyl or haloalkyl; R8, R9 are H or alkyl optionally substituted with halogen, alkoxy or haloalkoxy; Q is a saturated or unsatd. chain optionally containing one to three heteroatoms O, S(O)0-2, NH, alkylimino, cycloalkylimino, etc.; W is OH, NHS(O)1-2R12, where R12 is alkyl, cycloalkyl, aryl or heterocyclyl] or their pharmaceutically-acceptable enantiomers, diastereomers, salts, solvates or prodrugs and methods for using them to inhibit the hepatitis C virus (HCV). Thus, cyclic peptide II (Boc = tert-butoxycarbonyl) was prepared via peptide coupling and olefin metathesis cyclization reactions and showed IC50 and EC50 values <0.05 μ M in the HCV NS3/4A protease inhibition assay. Combination studies showed that treatment of replicon cells with an HCV NS3 protease inhibitor, compound II and Intron A and/or inhibitors targeting HCV NS5A and/or NS5B, yield additive to synergistic antiviral effects.

IC ICM C07K

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 63

IT 1075-11-2P 2438-38-2P, Cyclohexanesulfonamide 3336-60-5P, 1 Chloro 4 methoxyisoquinoline 16027-16-0P 16955-87-6P 20117-47-9P, 1 Methylcyclobutanol 24188-72-5P 24188-73-6P 24188-74-7P 24188-79-2P 24188-80-5P 26829-43-6P 26829-47-0P 29526-99-6P, 1 Methylcyclopropanol 31053-32-4P 40682-54-0P 52989-50-1P 53533-54-3P 57250-87-0P 61040-20-8P 63132-85-4P 70810-23-0P 70810-24-1P 73945-39-8P, Cyclopentanesulfonamide 77077-83-9P 89641-80-5P 90359-73-2P 106462-85-5P 118313-35-2P 132997-77-4P 154350-29-5P, Cyclopropanesulfonamide 178153-11-2P 214045-86-0P 259214-54-5P 300831-40-7P 300831-41-8P 350498-77-0P 410086-25-8P 410086-27-0P 445305-91-9P, Cyclobutanesulfonamide 552335-43-0P 552335-44-1P 552335-45-2P 552335-46-3P 552335-47-4P 552335-54-3P 552335-55-4P 630421-42-0P 630421-67-9P 630421-82-8P 630421-85-1P 630421-88-4P 630421-91-9P 630422-13-8P 630422-14-9P 630422-15-0P 630422-16-1P 630422-17-2P 630422-19-4P 630422-20-7P 630422-21-8P

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790305-07-6P	790305-08-7P	790305-09-8P	790305-10-1P	790305-11-2P
790305-12-3P				

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of macrocyclic isoquinoline peptide inhibitors of hepatitis C virus)

IT **630423-01-7P**

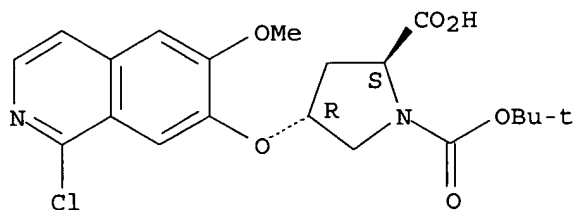
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of macrocyclic isoquinoline peptide inhibitors of hepatitis C virus)

RN 630423-01-7 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(1-chloro-6-methoxy-7-isoquinolinyl)oxy]-, 1-(1,1-dimethylethyl) ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 7 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:569862 CAPLUS

DOCUMENT NUMBER: 141:123901

TITLE: Preparation of N-sulfonyl-cyclic amine-2-carbohydroxamic acid derivatives as metalloprotease inhibitors

INVENTOR(S): Natchus, Michael George; De, Biswanath; Pikul, Stanislaw; Almstead, Neil Gregory; Bookland, Roger Gunnard; Taiwo, Yetunde Olabisi; Cheng, Menyan

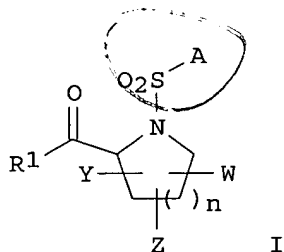
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 186,531.
CODEN: USXXCO

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004138260	A1	20040715	US 2003-730572	20031208
US 6417219	B1	20020709	US 1997-918317	19970826
US 2002061877	A1	20020523	US 2001-888675	20010625
US 6569855	B2	20030527		
US 2002072517	A1	20020613	US 2001-888759	20010625
US 2003105153	A1	20030605	US 2002-186531	20020701
US 6872742	B2	20050329		
US 2003191163	A1	20031009	US 2002-308780	20021203
US 6858628	B2	20050222		
JP 2004115531	A2	20040415	JP 2003-384116	20031113
US 2005101567	A1	20050512	US 2004-3594	20041203
US 2005154019	A1	20050714	US 2004-3884	20041203
PRIORITY APPLN. INFO.:			US 1996-24842P	P 19960828
			US 1997-918317	A3 19970826
			US 2001-888675	A2 20010625
			US 2001-888759	B2 20010625
			US 2002-186531	A2 20020701
			JP 1998-511715	A3 19970822
			US 2002-308780	A3 20021203

OTHER SOURCE(S): MARPAT 141:123901
 GI



AB The invention provides compds. according to formula (I), in particular N-sulfonylpyrrolidine-2-carboxylic acid derivs., [wherein A = each (un)substituted alkyl, heteroalkyl, aryl, or heteroaryl; R1 = NHOR2 (where R2 = H, alkyl); W = one or more of H, lower alkyl, or an alkylene bridge that forms a ring in addition to the main ring; Y = independently one or more of HO, SR3, SOR4, SO2R8, alkoxy, or (un)substituted amino (where R8 = alkyl, aryl, heteroaryl, heteroalkyl, amino, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino); Z = H, HO, or alkyl, or an alkylene or heteroalkylene bridge that forms a ring in addition to the main ring; n = 1; some provisos applied], pharmaceutically-acceptable salts, biohydrolyzable amides, esters, or imides thereof are prepared These compds. are useful as inhibitors of metalloproteases, and effective in treating conditions characterized by excess activity of these enzymes, in particular restenosis. Thus, cis-hydroxy-D-propine was condensed with 4-methylphenylsulfonyl chloride in the presence of Et3N and 2,6-dimethylpyridine in aqueous dioxane at room temperature for 14 h gave N-(4-methylphenylsulfonyl)-cis-hydroxy-D-propine which was esterified with

MeOH and SOCl₂ to give N-(4-methylphenylsulfonyl)-cis-hydroxy-D-propine Me ester which was treated with hydroxylamine monopotassium salt in MeOH overnight to give (2R,4S)-1-(4-Methoxyphenylsulfonyl)-2-(N-hydroxycarboxamido)-4S-hydroxypyrrolidine.

IC ICM A61K031-445

ICS A61K031-454; A61K031-4025; A61K031-4015

INCL 514317000; 514326000; 514422000; 514423000

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 7

IT 1138-54-1P, 4-(Isobutoxy)phenylsulfonyl chloride 57850-07-4P,
1-(4-Methylphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine
64700-65-8P, (2R)-2-Methoxycarbonyl-5-pyrrolidinone 182937-63-9P,
(2R)-2-Benzoyloxy-3-phenylpropanoic acid 203934-42-3P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-4-oxopyrrolidine
203934-63-8P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-
hydroxypyrrolidine 203994-66-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-
carboxy-(4R)-hydroxypyrrolidine 203994-80-3P, 1-(4-
Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine
203994-82-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-
acetylthiopyrrolidine 204072-15-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-
carbomethoxy-(4S)-benzoyloxypyrrolidine 204072-16-2P,
1-(4-Methoxyphenylsulfonyl)-(2S)-carbomethoxy-(4R)-hydroxypyrrolidine
204072-17-3P, 1-(4-Methoxyphenylsulfonyl)-(2S)-carbomethoxy-(4S)-
hydroxypyrrolidine 204072-18-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-
carboxy-(4S)-hydroxypyrrolidine 204072-19-5P, 1-(4-
Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-methoxypyrrolidine
204072-20-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-
[(trifluoromethanesulfonyl)oxy]pyrrolidine 204072-21-9P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(2-
benzothiazolylthio)pyrrolidine 204072-22-0P, 1-(4-Methoxyphenylsulfonyl)-
(2R)-carbomethoxy-(4S)-hydroxypyrrolidine 204072-23-1P,
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benzothiazolylthio)pyrrolidine 204072-24-2P, 1-(4-Methoxyphenylsulfonyl)-
(2R)-carbomethoxy-(4S)-(1-methyl-2-imidazolylthio)pyrrolidine
204072-25-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-(1-methyl-
2-imidazolylthio)pyrrolidine 204072-26-4P, 1-(4-Methoxyphenylsulfonyl)-
(2R)-carbomethoxy-(4S)-phenoxypyrrolidine 204072-27-5P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[4-
(benzyloxy)phenoxy]pyrrolidine 204072-28-6P,
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phenylaminophenoxy)pyrrolidine 204072-29-7P, 1-(4-Methoxyphenylsulfonyl)-
(2R)-carbomethoxy-(4S)-(3-pyridinyloxy)pyrrolidine 204072-30-0P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-phenylthiopyrrolidine
204072-32-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(4-
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(2R)-carbomethoxy-(4S)-(3-methoxyphenylthio)pyrrolidine 204072-36-6P,
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1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-[(2-
methoxyethoxy)methoxy]pyrrolidine 204072-39-9P 204072-40-2P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carboxy-4-oxopyrrolidine 204072-41-3P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-4-hydroxy-4-
ethylpyrrolidine 204072-42-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-
carbomethoxy-(4R)-4-hydroxy-4-phenylpyrrolidine 204072-44-6P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-3,3-dimethyl-4-
oxopyrrolidine 204072-45-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-
carbomethoxy-3,3-dimethyl-(4R)-hydroxypyrrolidine 204072-46-8P,
1-(3,4-Dimethoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine
204072-47-9P, 1-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-

hydroxypyrrolidine 204072-50-4P, 1-(4-Bromobenzenesulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 204072-51-5P, 1-(2-Methyl-4-bromobenzenesulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 204072-52-6P, 1-(2,4-Dichlorophenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 204072-53-7P, 4-(2-Methoxyethoxy)phenylsulfonyl chloride 204072-56-0P, 1-(4-Isobutyloxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 204072-57-1P, 1-(2-Methyl-4-bromophenylsulfonyl)-(2R)-carbomethoxy-(4S)-(3-methoxyphenylthio)pyrrolidine 204072-58-2P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(2-benzothiazolylthio)pyrrolidine 204072-59-3P, 1-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(2-benzothiazolylthio)pyrrolidine 204072-60-6P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(4-methoxyphenylthio)pyrrolidine 204072-61-7P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(3-pyridyloxy)pyrrolidine 204072-62-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-azidopyrrolidine 204072-63-9P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-aminopyrrolidine 204072-64-0P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-methylsulfonyloxypyrrolidine 204072-65-1P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-azidopyrrolidine 204072-66-2P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-aminopyrrolidine 204072-67-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-propylaminopyrrolidine 204072-68-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(hexylamino)pyrrolidine 204072-69-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(2-phenylethylamino)pyrrolidine 204072-70-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(N-butyl-N-hexylamino)pyrrolidine 204072-71-9P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[(methanesulfonyl)amino]pyrrolidine 204072-72-0P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[(methanesulfonyl)amino]pyrrolidine 204072-74-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(3-pyridylmethyl)amino]pyrrolidine 204072-75-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(3-pyridylmethyl)-N-(methanesulfonyl)amino]pyrrolidine 204072-76-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[bis(methanesulfonyl)amino]pyrrolidine 204072-77-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(methanesulfonyl)-N-propylamino]pyrrolidine 204072-78-6P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[(4-methoxyphenylsulfonyl)amino]pyrrolidine 204072-79-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(hexanoylamino)pyrrolidine 204072-81-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[(methylcarbamoyl)amino]pyrrolidine 204072-82-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-benzyloxypropyl)amino]pyrrolidine 204072-83-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-benzyloxy-3-phenylpropyl)amino]pyrrolidine 204072-84-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-benzyloxypropyl)-N-propylamino]pyrrolidine 204072-85-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-hydroxypropyl)-N-propylamino]pyrrolidine 204072-86-6P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-benzyloxy-3-phenylpropyl)-N-propylamino]pyrrolidine 204072-87-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-hydroxy-3-phenylpropyl)-N-propylamino]pyrrolidine 204072-88-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(1-piperidyl)pyrrolidine 204072-89-9P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(1-piperidyl)pyrrolidine 204072-90-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(morpholino)pyrrolidine 204072-91-3P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(morpholino)pyrrolidine 204072-92-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204072-93-5P,

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 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(4-biphenylamino)pyrrolidine 722550-48-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-(methanesulfonyl)pyrrolidine 722550-49-4P,
 1-[4-(2-Methoxyethyl)phenylsulfonyl]-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 722550-52-9P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-5-pyrrolidinone 722550-53-0P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carboxy-5-pyrrolidinone 722550-54-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-benzyloxycarboxamido)-5-pyrrolidinone
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid as metalloprotease inhibitors for treatment of restenosis)

IT 204072-28-6P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(3-phenylaminophenoxy)pyrrolidine

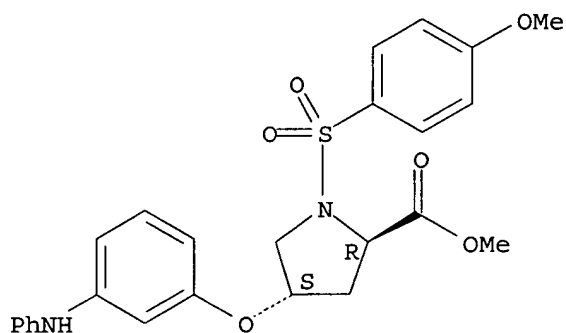
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid as metalloprotease inhibitors for treatment of restenosis)

RN 204072-28-6 CAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[3-(phenylamino)phenoxy]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 8 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:430698 CAPLUS

DOCUMENT NUMBER: 141:7017

TITLE: Preparation of sulfonamides as antagonists of urotensin II

INVENTOR(S): Dodson, Jason W.; Ghavimi-Alagha, Bahman; Girard, Gerald R.; King, Bryan W.; McAtee, John Jeffrey; Neeb, Michael J.; Wang, Ning; Yuan, Catherine C. K.

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 82 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

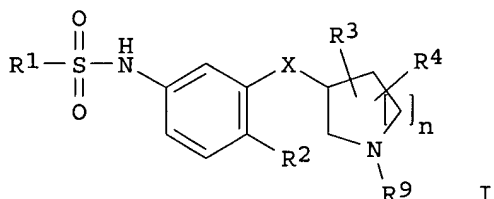
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043366	A2	20040527	WO 2003-US35307	20031106
WO 2004043366	A3	20040715		

W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, EG, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SC, SG, TN, TT, UA, US, UZ, VN, YU, ZA

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-424058P P 20021106
US 2002-424215P P 20021106

OTHER SOURCE(S): MARPAT 141:7017
GI



AB The title compds. [I; R1 = (un)substituted Ph, thienyl, furanyl, etc.; R2 = H, halo, CF3, CN, alkyl; R3, R4 = H, alkyl, PhCH2, etc.; R9 = H, alkyl, (CH2)mR15; R15 = Ph, OH, CO(alkyl); m = 1-2; n = 0-2; X = O, S, CH2], useful as antagonists of urotensin II, were prepared and formulated. E.g., a multi-step synthesis of N-{3-[2(S)-hydroxymethyl-1-methylpyrrolidin-3(R)-yloxy]-4-trifluoromethylphenyl}-2-bromo-4,5-dimethoxybenzenesulfonamide which showed Ki of 21 nM in h-U-II radioligand binding assay, was given.

IC ICM A61K

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 63

IT 694511-62-1P 694511-63-2P 694513-20-7P 694514-26-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of sulfonamides as antagonists of urotensin II)

IT	474960-93-5P	694471-98-2P	694471-99-3P	694472-00-9P	694472-07-6P
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	694511-79-0P	694511-80-3P	694511-81-4P	694511-82-5P	694511-83-6P
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694513-08-1P	694513-09-2P	694513-10-5P	694513-12-7P	694513-14-9P
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694513-72-9P	694513-75-2P	694513-78-5P	694513-81-0P	694513-83-2P
694513-86-5P	694513-89-8P	694513-92-3P	694513-95-6P	694513-97-8P
694513-99-0P	694514-01-7P	694514-03-9P	694514-04-0P	694514-05-1P
694514-07-3P	694514-10-8P	694514-12-0P	694514-31-3P	

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of sulfonamides as antagonists of urotensin II)

IT 393-15-7P 1682-10-6P 52427-05-1P 53935-71-0P 55854-45-0P
 69411-67-2P 81597-51-5P 100367-48-4P 106877-20-7P 154065-10-8P
 474937-62-7P 694472-01-0P 694472-02-1P 694472-04-3P 694472-05-4P
694511-59-6P 694511-60-9P 694511-61-0P
 694514-16-4P 694514-18-6P 694514-19-7P 694514-20-0P 694514-21-1P
 694514-22-2P 694514-23-3DP, resin bound 694514-24-4P 694514-25-5P
694514-27-7P 694514-29-9P 694514-30-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

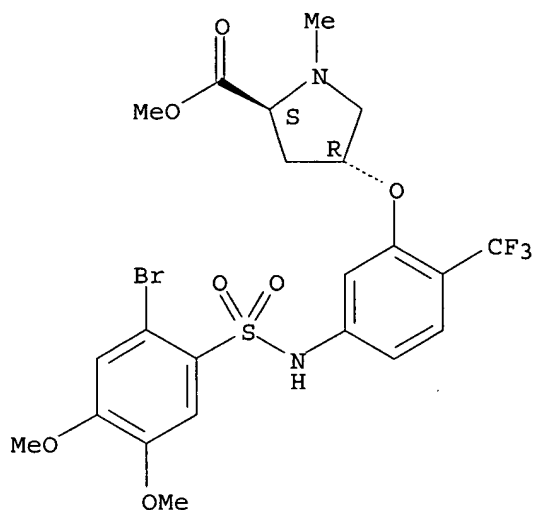
(preparation of sulfonamides as antagonists of urotensin II)

IT **694511-62-1P 694514-26-6P**
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of sulfonamides as antagonists of urotensin II)

RN 694511-62-1 CAPLUS

CN L-Proline, 4-[5-[(2-bromo-4,5-dimethoxyphenyl)sulfonyl]amino]-2-(trifluoromethyl)phenoxy]-1-methyl-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

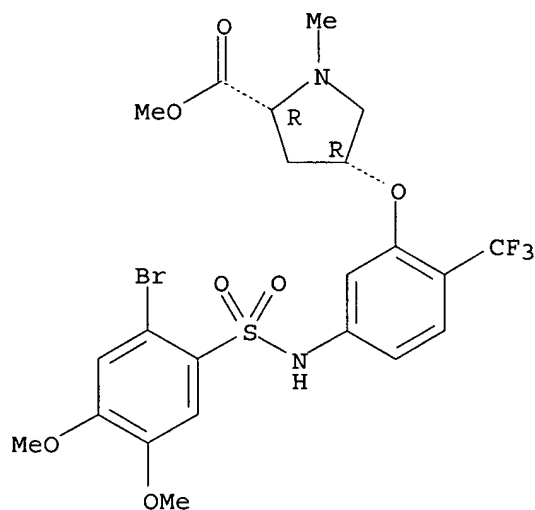
Absolute stereochemistry.



RN 694514-26-6 CAPLUS

CN D-Proline, 4-[5-[[2-bromo-4,5-dimethoxyphenyl)sulfonyl]amino]-2-(trifluoromethyl)phenoxy]-1-methyl-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 694513-29-6P 694513-31-0P

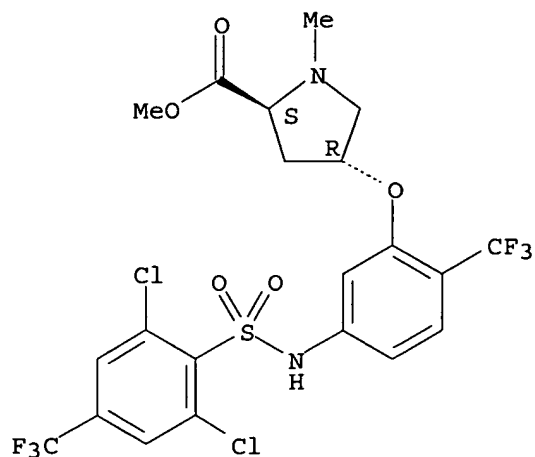
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of sulfonamides as antagonists of urotensin II)

RN 694513-29-6 CAPLUS

CN L-Proline, 4-[5-[[2,6-dichloro-4-(trifluoromethyl)phenyl)sulfonyl]amino]-2-(trifluoromethyl)phenoxy]-1-methyl-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

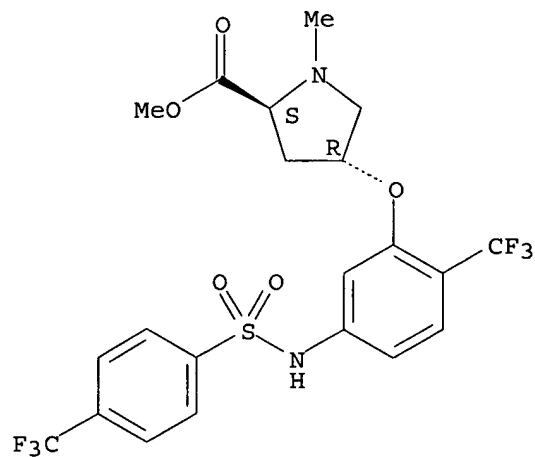
Absolute stereochemistry.



RN 694513-31-0 CAPLUS

CN L-Proline, 1-methyl-4-[2-(trifluoromethyl)-5-[[[4-(trifluoromethyl)phenyl]sulfonyl]amino]phenoxy]-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



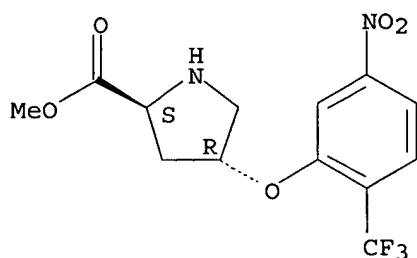
IT 694511-59-6P 694511-60-9P 694511-61-0P
694514-27-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of sulfonamides as antagonists of urotensin II)

RN 694511-59-6 CAPLUS

CN L-Proline, 4-[5-nitro-2-(trifluoromethyl)phenoxy]-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

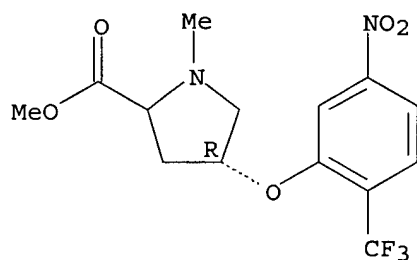
Absolute stereochemistry.



RN 694511-60-9 CAPLUS

CN Proline, 1-methyl-4-[5-nitro-2-(trifluoromethyl)phenoxy]-, methyl ester,
(4R)- (9CI) (CA INDEX NAME)

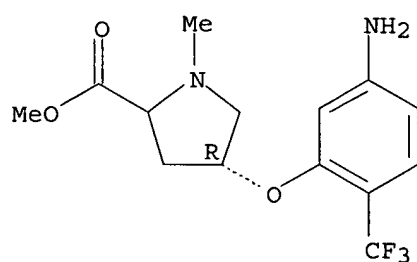
Absolute stereochemistry.



RN 694511-61-0 CAPLUS

CN Proline, 4-[5-amino-2-(trifluoromethyl)phenoxy]-1-methyl-, methyl ester,
(4R)- (9CI) (CA INDEX NAME)

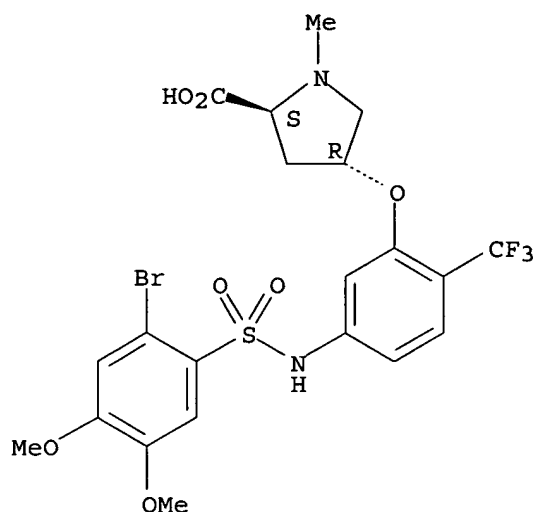
Absolute stereochemistry.



RN 694514-27-7 CAPLUS

CN L-Proline, 4-[5-[[[2-bromo-4,5-dimethoxyphenyl)sulfonyl]amino]-2-(trifluoromethyl)phenoxy]-1-methyl-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 9 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:392321 CAPLUS

DOCUMENT NUMBER: 140:406826

TITLE: Preparation of N-benzylpiperazine derivatives as chemokine receptor CCR1 antagonists useful as immunomodulatory agents

INVENTOR(S): Blumberg, Laura C.; Brown, Matthew F.; Gaweco, Anderson S.; Gladue, Ronald P.; Hayward, Matthew M.; Lundquist, Gregory D.; Poss, Christopher S.; Shavnya, Andrei

PATENT ASSIGNEE(S): Pfizer Inc, USA

SOURCE: U.S. Pat. Appl. Publ., 58 pp.

CODEN: USXXCO

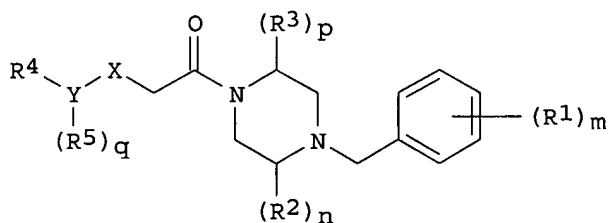
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004092529	A1	20040513	US 2003-686993	20031016
PRIORITY APPLN. INFO.: OTHER SOURCE(S): GI	MARPAT 140:406826		US 2002-422590P	P 20021030



I

AB The present invention relates to compds. of the formula (I) and the

pharmaceutically acceptable forms thereof [m = 0-5; n, p = 0-2; q = 0-4; X = O, S, CH₂, (un)substituted NH; Y = C₆-10 aryl, C₂-9 heteroaryl; R₁ = H, HO, halo, C₁-8 alkyl, C₁-8 alkoxy, HO-C₁-8 alkyl, cyano, NH₂, H₂N-C₁-8 alkyl, CO₂H, C₁-8 alkyl-CO, C₁-8 alkyl-CO-C₁-8 alkyl, CONH₂, or H₂NCO-C₁-8 alkyl; R₂, R₃ = H, oxo, C₁-8 alkyl, C₃-8 cycloalkyl-C₁-8 alkyl, C₆-10 aryl, C₆-10 aryl-C₁-8 alkyl, HO-C₁-8 alkyl, C₁-8 alkyl-O-C₁-8 alkyl, H₂N-C₁-8 alkyl, C₁-8 alkyl-NH-C₁-8 alkyl, (C₁-8 alkyl)₂N-C₁-8 alkyl, C₂-9 heterocyclyl-C₁-8 alkyl, C₃-8 cycloalkyl-NH-C₁-8 alkyl, C₁-8 alkyl-CO-NH-C₁-8 alkyl-O-CO-NH-C₁-8 alkyl, H₂NCO-NH-C₁-8 alkyl, C₁-8 alkyl-SO₂NH-C₁-8 alkyl, C₂-9 heteroaryl-C₁-8 alkyl, H₂NCO, H₂NCO-C₁-8 alkyl; R₄ = (HO₂C)(H₂N)-C₁-8 alkyl, (HO₂C)[(C₁-8 alkyl)NH]-C₁-8 alkyl, (HO₂C)[(C₁-8 alkyl)₂N]-C₁-8 alkyl, (HO₂C-C₁-8 alkyl)(C₁-8 alkyl)N, (HO₂C-C₁-8 alkyl)(C₁-8 alkyl)N-C₁-8 alkyl, (HO₂C-C₁-8 alkyl)(C₁-8 alkyl-SO₂)N, (HO₂C-C₁-8 alkyl)(C₁-8 alkyl-SO₂)N-C₁-8 alkyl, (HO₂C-C₁-8 alkyl)(C₁-8 alkyl-CO)N, etc.; R₅ = H, HO, halo, cyano, CO₂H, H₂N, C₁-8 alkyl-NH, (C₁-8 alkyl)₂N, C₁-8 alkyl, C₁-8 alkyl-O, HO-C₁-8 alkyl, C₁-8 alkyl-NH-C₁-8 alkyl, (C₁-8 alkyl)₂N-C₁-8 alkyl, etc.]. Moreover, the present invention is also directed at pharmaceutical compns. comprising the compound I and a pharmaceutically acceptable carrier. Furthermore, the present invention is directed at methods of using the herein described compds. and compns. for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal. Particularly, disclosed is a method of treating or preventing a disorder or condition selected from the group consisting of fibrosis, Alzheimer's disease, conditions associated with leptin production, sequelae associated with cancer, cancer metastasis, diseases or conditions related to production of cytokines at inflammatory sites, and tissue damage caused by inflammation induced by infectious agents, wherein the method comprises administering to a mammal in need of such treatment or prevention a pharmaceutically effective amount of the compound I or a pharmaceutically acceptable form thereof. The compds. I are potent and selective inhibitors of MIP-1 α (CCL3) binding to its receptor CCR1 found on inflammatory and immunomodulatory cells (preferably leukocytes and lymphocytes). [2-[3-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methylphenoxy]acetic acid was condensed with methanesulfonamide in CH₂Cl₂ at room temperature for 18 h using 4-dimethylaminopyridine and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride to give N-[[2-[3-[4-(4-fluoro-benzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxo-propyl]-5-methylphenoxy]acetyl]methanesulfonamide. All the compds. I inhibited MIP-1 α (and the related chemokines shown to interact with CCR1) induced chemotaxis of THP-1 cells and human leukocytes with IC₅₀ of <10 μ M.

IC ICM A61K031-495

INCL 514255010

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 7035-10-1P, (5-Chloro-2-Methoxy-Phenyl)-Methanol 7035-11-2P,
4-Chloro-2-chloromethyl-1-methoxybenzene 7048-38-6P,
(5-Chloro-2-Methoxy-Phenyl)-Acetonitrile 7417-89-2P,
(4-Chloro-2-hydroxyphenoxy)acetic acid 7569-62-2P, (5-Chloro-2-methoxyphenyl)acetic acid 24161-38-4P, (5-Chloro-2-hydroxyphenyl)acetic acid 25032-64-8P, 4-Chloro-But-3-Enenitrile 27130-43-4P,
4-Chlorobut-2-enenitrile 56913-08-7P, (4-Chloro-2-methoxyphenoxy)acetic acid 62903-23-5P, 4-(5-Chloro-2-Hydroxy-Phenyl)-4-Oxo-Butyric acid 66497-42-5P, 3-Hydroxy-6-Methyl-Pyridine-2-carboxaldehyde 76322-41-3P,
(5-Chloro-2-hydroxyphenyl)acetic acid ethyl ester 82020-51-7P,
5-Chloro-2-Methoxy-Benzenesulfonamide 82020-64-2P, 5-Chloro-2-Hydroxy-Benzenesulfonamide 86658-86-8P, (Dimethoxymethyl)diphenylphosphine oxide 100119-68-4P, 4-(5-Chloro-2-Hydroxy-Phenyl)-4-Oxo-Butyric Acid Ethyl Ester 131803-48-0P, 6-Bromomethyl-Nicotinic Acid Methyl Ester 176433-49-1P,

2,5-Dichloro-Pyridine-3-carboxaldehyde 217645-80-2P,
5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzaldehyde 217648-11-8P, 2-Chloro-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 329219-99-0P,
7-Chlorobenzo[1,4]dioxin-2-one 331729-64-7P, 2-(5-Chloro-2-Hydroxy-Benzyl)-Isoindole-1,3-Dione 364066-89-7P, (S)-2-(4-Fluoro-benzylamino)-propionic Acid methyl ester 364066-90-0P, (2S)-2-[(2R)-(2-tert-Butoxycarbonylamino-propionyl)(4-fluoro-benzyl)-amino]propionic acid methyl ester 364066-91-1P, (3R,6S)-1-(4-Fluoro-benzyl)-3,6-dimethyl-piperazine-2,5-dione 364066-97-7P, 2-(4-Chloro-2-Nitro-Phenoxy)-1-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-Ethanone 364066-98-8P, 2-(2-Amino-4-Chloro-Phenoxy)-1-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-Ethanone 364067-02-7P, 2-(2-Aminomethyl-4-Chloro-Phenoxy)-1-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-Ethanone 422270-29-9P, (3R)-1-(4-Fluoro-Benzyl)-3-Methyl-Piperazine 422270-30-2P, 2-Chloro-1-[4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-Piperazin-1-yl]-Ethanone 422270-31-3P, 2-(4-Chloro-2-Nitro-Phenoxy)-1-[4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-Piperazin-1-yl]-Ethanone 422270-32-4P, 2-(2-Amino-4-Chloro-Phenoxy)-1-[4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-Piperazin-1-yl]-Ethanone 478833-41-9P, (2R,5S)-1-(4-Fluorobenzyl)-2,5-dimethylpiperazine 478833-49-7P, 2-(4-Chloro-2-Hydroxymethyl-Phenoxy)-1-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-Ethanone 478833-52-2P, 2-(4-Chloro-2-chloromethylphenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 478833-90-8P, [5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Acetic acid Ethyl Ester 519171-78-9P, 1-[4-(4-Fluoro-benzyl)-(2R,5S)-2,5-dimethyl-piperazin-1-yl]-3-(2-hydroxy-4-methyl-phenyl)-propan-1-one 519171-79-0P, [2-[3-[4-(4-Fluoro-benzyl)-(2R,5S)-2,5-dimethyl-piperazin-1-yl]-3-oxo-propyl]-5-methyl-phenoxy]-acetic acid methyl ester 519171-82-5P, 2-(4-Chloro-2-hydroxy-phenoxy)-1-[4-(4-fluoro-benzyl)-(2R,5S)-2,5-dimethyl-piperazin-1-yl]-ethanone 519171-83-6P, [5-Chloro-2-[2-[4-(4-fluoro-benzyl)-(2R,5S)-2,5-dimethyl-piperazin-1-yl]-2-oxo-ethoxy]-phenoxy]-acetic acid methyl ester 519171-86-9P, (2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-Dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid ethyl ester 519171-88-1P, 4-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-4-Oxo-Butyric acid Ethyl Ester 519171-90-5P, [5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Carbamic Acid 4-Nitro-Phenyl Ester 519171-91-6P, 3-[3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Ureido]-Propionic acid Methyl Ester 519171-94-9P, 3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzylamino]-Propionic acid Methyl Ester 519171-97-2P, 2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzyl]-Isoindole-1,3-Dione 519172-01-1P, [5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzyl]-Acetic acid tert-Butyl Ester 519172-03-3P, [5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzyl]-Acetic Acid 519172-05-5P, 1-(tert-Butoxycarbonyl)-1-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzyl]Sulfamide 519172-08-8P, [5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Acetic Acid 519172-11-3P, 3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Acrylic acid Ethyl Ester 519172-12-4P, 3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Propionic acid Ethyl Ester 519172-13-5P, 3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Propionic Acid 519172-17-9P, 5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzenesulfonamide 519172-18-0P, N-(tert-Butoxycarbonyl)-5-

Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzenesulfonamide 519172-19-1P 519172-23-7P, Acetic acid 2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzenesulfonylamino]-1,1-Dimethyl-2-Oxo-Ethyl Ester 519172-25-9P, Thioacetic Acid S-(5-Chloro-2-Methoxy-Benzyl) Ester 519172-26-0P, (5-Chloro-2-Methoxy-Phenyl)-Methanesulfonic Acid 519172-27-1P, (5-Chloro-2-Methoxy-Phenyl)-Methanesulfonamide 519172-28-2P, (5-Chloro-2-Hydroxy-Phenyl)-Methanesulfonamide 519172-29-3P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519172-31-7P, Acetic acid 2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenylmethanesulfonylamino]-1,1-Dimethyl-2-Oxo-Ethyl Ester 519172-34-0P, 1-[4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-Piperazin-1-yl]-2-Hydroxy-Ethanone 519172-35-1P, (R)-2-(5-Chloro-3-Nitro-Pyridin-2-yloxy)-1-[4-(4-Fluoro-Benzyl)-2-Methyl-Piperazin-1-yl]-Ethanone 519172-36-2P, 2-(3-Amino-5-Chloro-Pyridin-2-yloxy)-1-[4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-Piperazin-1-yl]-Ethanone 519172-39-5P, (2,5-Dichloro-Pyridin-3-yl)-Acetic Acid Methyl Ester 519172-41-9P, [5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Pyridin-3-yl]-Acetic acid Methyl Ester 519172-43-1P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]acetic acid 519172-46-4P, 5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Pyridine-3-carboxaldehyde 519172-47-5P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]acrylic acid ethyl ester 519172-48-6P, 3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Pyridin-3-yl]-Propionic acid Ethyl Ester 519172-50-0P, [2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethyl]-Carbamic Acid tert-Butyl Ester 519172-51-1P, 2-Amino-1-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-Ethanone 519172-52-2P, 5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethylamino]-Nicotinic Acid Methyl Ester 519172-53-3P, 5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethylamino]-Nicotinic Acid hydrochloride 519172-54-4P, [[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethylamino]-Pyridine-3-Carbonyl]-Amino]-Acetic acid Methyl Ester 519172-56-6P, 6-Chloro-3,3-Dimethyl-Benzo[1,4]Oxathiin-2-One 519172-58-8P, 2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenylsulfanyl]-2-Methyl-Propionic acid Ethyl Ester 519172-60-2P, 2-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]sulfonyl]-2-methylpropionic acid ethyl ester 519172-61-3P, 2-(5-Chloro-2-hydroxyphenylsulfanyl)-2-Methyl-Propionic acid Ethyl Ester 519172-63-5P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylsulfanyl]acetic acid methyl ester 519172-66-8P, 3-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-6-Methyl-Pyridine-2-carboxaldehyde 519172-67-9P, 3-[3-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-6-Methyl-Pyridin-2-yl]-Acrylic Acid Ethyl Ester 519172-68-0P, 3-[3-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethylpiperazin-1-yl]-2-Oxo-Ethoxy]-6-Methyl-Pyridin-2-yl]-Propionic Acid Ethyl Ester 519172-69-1P, 3-[3-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-6-Methyl-Pyridin-2-yl]-Propionic Acid sodium salt 519172-71-5P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-2-nitropropionic acid ethyl ester 519172-72-6P, 2-Amino-3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Propionic acid Ethyl Ester 519172-74-8P, [[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzyl]-Methyl-Amino]-Acetic acid Methyl

Ester 519172-79-3P, [2-(4-Fluoro-Benzylamino)-Ethyl]-Carbamic Acid
 tert-Butyl Ester 519172-80-6P, 4-[(2-tert-Butoxycarbonylamino-Ethyl)(4-
 Fluoro-Benzyl)-Amino]-But-2-Enoic acid Methyl Ester 519172-81-7P,
 (R)-[4-(4-Fluorobenzyl)piperazin-2-yl]acetic acid methyl ester
 519172-82-8P, 2-[(2R)-1-[(4-Chloro-2-Hydroxy-Phenoxy)-Acetyl]-4-(4-Fluoro-
 Benzyl)-Piperazin-2-yl]-Acetamide 519172-83-9P, [2-[2-[(2R)-2-
 Carbamoylmethyl-4-(4-Fluoro-Benzyl)-Piperazin-1-yl]-2-Oxo-Ethoxy]-5-Chloro-
 Phenoxy]-Acetic Acid tert-Butyl Ester **519172-84-0P**,
 (4S)-4-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-
 1-yl]-2-Oxo-Ethoxy]-Phenoxy]-Pyrrolidine-1,2S-Dicarboxylic acid
 Di-tert-Butyl Ester 519172-89-5P, 6-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-
 (2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenoxy]methyl]-
 Nicotinic acid Methyl Ester 519172-91-9P, 5-(5-Chloro-2-Hydroxy-Phenyl)-
 5-Oxo-Pentanoic Acid Ethyl Ester 519172-93-1P, 5-[5-Chloro-2-[2-[4-(4-
 Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-
 5-Oxo-Pentanoic acid Ethyl Ester 519172-98-6P, 2-(5-Chloro-3-Nitro-
 Pyridin-2-yloxy)-1-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-
 yl]Ethanone 519172-99-7P, 2-(3-Amino-5-chloropyridin-2-yloxy)-1-[4-(4-
 fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 519173-00-3P,
 4-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-
 2-Oxo-Ethoxy]-Pyridin-3-ylamino]-Butyric acid Ethyl Ester 519173-01-4P,
 [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-
 oxoethoxy]pyridin-3-ylamino]acetic acid ethyl ester 519173-04-7P,
 2-(4-Chloro-2-Hydroxy-Phenoxy)-1-[4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-
 Piperazin-1-yl]-Ethanone 519173-05-8P, 2-(4-Chloro-2-Cyanato-Phenoxy)-1-
 [4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-Piperazin-1-yl]-Ethanone
 519173-08-1P, 2-(4-Chloro-2-Isoxazol-5-yl-Phenoxy)-1-[4-(4-Fluoro-Benzyl)-
 (2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-Ethanone 519173-09-2P,
 3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-
 2-Oxo-Ethoxy]-Phenyl]-3-Oxo-Propionitrile 519173-11-6P,
 4-(5-Chloro-2-Hydroxy-Phenyl)-4-Oxo-Butyronitrile 519173-12-7P,
 4-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-
 2-Oxo-Ethoxy]-Phenyl]-4-Oxo-Butyronitrile 688032-00-0P,
 [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-
 oxoethoxy]benzyl]sulfonyl]acetic acid methyl ester 689256-99-3P,
 3-[3-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-
 oxoethoxy]-6-methylpyridin-2-yl]propionic acid 689257-00-9P,
 [5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-
 Oxo-Ethoxy]-Phenyl]-Acetonitrile
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(intermediate; preparation of N-benzylpiperazine derivs. as chemokine
 receptor CCR1 antagonists useful as immunomodulatory agents)

IT 519171-85-8P, (2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 Dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid 519171-87-0P,
 4-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-
 2-Oxo-Ethoxy]-Phenyl]-4-Oxo-Butyric Acid **519172-85-1P**,
 (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-
 yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid dihydrochloride
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of N-benzylpiperazine derivs. as chemokine receptor CCR1
 antagonists useful as immunomodulatory agents)

IT 519171-77-8P, N-[[2-[3-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-
 yl]-3-oxopropyl]-5-methylphenoxy]acetyl]methanesulfonamide 519171-81-4P,
 N-[[5-Chloro-2-[2-[4-(4-fluoro-benzyl)-(2R,5S)-2,5-dimethyl-piperazin-1-
 yl]-2-oxo-ethoxy]-phenoxy]-acetyl]-methanesulfonamide hydrochloride
 519171-92-7P, [5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-
 Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]sulfamoyl]-Acetic Acid 519171-96-1P,

1-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzyl]-3-(2-Methylbenzenesulfonyl)-Urea 519171-98-3P,
(2-Methylbenzenesulfonyl)-Carbamic acid 5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzyl Ester
519171-99-4P, 2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzylsulfamoyl]-Propionic Acid
519172-00-0P, N-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzyloxy]-Acetyl]-Methanesulfonamide
519172-04-4P, 1-Acetyl-3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzyl]Sulfamide 519172-06-6P,
[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzylideneaminooxy]-Acetic Acid 519172-07-7P,
N-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Acetyl]-Methanesulfonamide 519172-09-9P,
N-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Acetyl]-Sulfamide 519172-10-2P,
N-[3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Propionyl]-Methanesulfonamide 519172-14-6P,
3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Acrylic Acid 519172-16-8P, [5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzenesulfonylamino]-Acetic Acid hydrochloride 519172-20-4P,
5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-N-[(2-Propylamino)Carbonyl]-Benzenesulfonamide 519172-21-5P,
5-Chloro-N-(2,2-Dimethyl-Propionyl)-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzenesulfonamide 519172-22-6P,
5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-N-(2-Hydroxy-2-Methyl-Propionyl)-Benzenesulfonamide
519172-24-8P, N-Acetyl-1-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Methanesulfonamide
519172-30-6P, 1-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-N-(2-Hydroxy-2-Methyl-Propionyl)-Methanesulfonamide 519172-33-9P, N-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Pyridin-3-yl]-Succinamic Acid
519172-37-3P, N-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Pyridin-3-yl]-Acetyl]-Methanesulfonamide
519172-45-3P, 3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Pyridin-3-yl]-Propionic Acid 519172-49-7P,
[[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethylamino]-Pyridine-3-Carbonyl]-Amino]-Acetic Acid 519172-55-5P,
2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenylsulfanyl]-2-Methyl-Propionic Acid 519172-59-9P,
2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzenesulfonyl]-2-Methyl-Propionic Acid 519172-62-4P,
[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenylmethanesulfonyl]-Acetic Acid 519172-65-7P,
N-[3-[3-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-6-Methyl-Pyridin-2-yl]-Propionyl]-Methanesulfonamide
519172-70-4P, 2-Amino-3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Propionic Acid
519172-73-7P, [[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzyl]-Methyl-Amino]-Acetic Acid
519172-75-9P, 2-[4-Chloro-2-(2H-Tetrazol-5-ylmethoxy)-Phenoxy]-1-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-Ethanone
519172-77-1P, 2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenoxy]-Nicotinic Acid hydrochloride
519172-78-2P, [2-[2-[(2R)-2-Carbamoylmethyl-4-(4-Fluoro-Benzyl)-Piperazin-1-yl]-2-Oxo-Ethoxy]-5-Chloro-Phenoxy]-Acetic Acid 519172-86-2P,
(4S)-4-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenoxy]-1-Methyl-Pyrrolidine-(2S)-2-Carboxylic Acid

dihydrochloride 519172-87-3P, 1-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-N-(Methoxycarbonyl)-Methanesulfonamide 519172-88-4P, 6-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenoxymethyl]-Nicotinic Acid 519172-90-8P, 5-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-5-Oxo-Pentanoic Acid 519172-94-2P, 5-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Dihydro-Furan-2-One 519172-97-5P, 4-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Pyridin-3-ylamino]-Butyric Acid acetate 519173-03-6P, [5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Pyridin-3-ylamino]-Acetic Acid acetate 519173-10-5P, 1-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-2-(1H-Tetrazol-5-yl)-Ethanone hydrochloride 519173-13-8P, 1-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-3-(1H-Tetrazol-5-yl)-Propan-1-One hydrochloride 519173-14-9P, [2-[3-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methoxyphenoxy]acetic acid 519173-15-0P, N-[[2-[3-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methoxyphenoxy]acetyl]methanesulfonamide 519173-16-1P, [5-Chloro-2-[3-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]phenoxy]acetic acid 519173-17-2P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-oxoacetic acid 519173-18-3P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-19-4P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-20-7P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-21-8P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-22-9P, [5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-23-0P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-24-1P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-25-2P, N-[[5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-26-3P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-27-4P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-28-5P, 6-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyridine-2-carboxylic acid 519173-29-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-30-9P, (2R)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-31-0P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-32-1P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-33-2P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-34-3P, (2S)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-35-4P, 2-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-36-5P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-37-6P, 2-[5-Bromo-2-[2-[4-

(4-fluorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy]phenoxy] -2-methylpropionic acid 519173-38-7P, [5-Bromo-2-[2-[4-(4-fluorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy]phenoxy]difluoroacetic acid 519173-39-8P, (2S) -2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy]phenoxy]butyric acid 519173-40-1P, (2S) -2-Amino-4-[5-bromo-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]butyric acid 519173-41-2P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]pyridine-2-carboxylic acid 519173-42-3P, N-[(2R) -2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]butyryl]methanesulfonamide 519173-43-4P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]methyl]thiazole-4-carboxylic acid 519173-44-5P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]methyl]furan-2-carboxylic acid 519173-45-6P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]methyl]furan-2-carboxylic acid 519173-46-7P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]methyl]thiophene-2-carboxylic acid 519173-47-8P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]methyl]furan-3-carboxylic acid 519173-48-9P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]methyl]thiophene-2-carboxylic acid 519173-49-0P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy]phenoxy]methyl]furan-2-carboxylic acid 519173-50-3P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl) -2-methylpiperazin-1-yl] -2-oxoethoxy]phenoxy]methyl]furan-2-carboxylic acid 519173-51-4P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy] -5-(2-methoxyethyl)pyrimidine-2,4,6-trione 519173-53-6P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy] -5-methylpyrimidine-2,4,6-trione 519173-55-8P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy] -5-ethylpyrimidine-2,4,6-trione 519173-58-1P, (2R) -2-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy]phenoxy]propionic acid 519173-60-5P, (2S) -2-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy]phenoxy]propionic acid 519173-62-7P, (4S) -4-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]pyrrolidine-2-carboxylic acid 519173-63-8P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy] -2,2-dimethylpropionic acid 519173-65-0P, (4S) -4-[5-Bromo-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]pyrrolidine- (2S) -2-carboxylic acid 519173-67-2P, (4S) -4-[5-Bromo-2-[2-[4-(4-fluorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy]phenoxy]pyrrolidine- (2S) -2-carboxylic acid 519173-69-4P, (4S) -4-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]pyrrolidine- (2S) -2-carboxylic acid 519173-70-7P, N-[(4S) -4-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]pyrrolidine- (2S) -2-carbonyl]methanesulfonamide 519173-72-9P, [3-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]ureido]acetic acid 519173-73-0P, 3-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]ureido]propionic acid 519173-74-1P, 3-[3-[4-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]ureido]propionic acid 519173-75-2P, [3-[4-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]ureido]acetic acid 519173-76-3P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl] -3-(methylsulfonyl)urea

519173-77-4P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylsulfamoyl]acetic acid
519173-78-5P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]-3-(methylsulfonyl)urea
519173-79-6P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]-3-(2-methylbenzoyl)sulfamide
519173-80-9P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylideneaminoxy]acetic acid
519173-81-0P, [1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ethylideneaminoxy]acetic acid
519173-82-1P, [1-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ethylideneaminoxy]acetic acid
519173-83-2P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]phenylmethyleaminoxy]acetic acid
519173-84-3P, [2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-methylbenzylideneaminoxy]acetic acid
519173-85-4P, (2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]propionic acid
519173-86-5P, (2R)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]propionic acid
519173-87-6P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]-2-methylpropionic acid
519173-88-7P, Methylsulfonylcarbamic acid 5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl ester
519173-89-8P, N-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzoyl]methanesulfonamide
519173-90-1P, N-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]benzoyl]methanesulfonamide
519173-91-2P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide
519173-92-3P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide
519173-93-4P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]-trifluoromethanesulfonamide
519173-94-5P
519173-95-6P, N-[[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-4-methoxyphenyl]acetyl]methanesulfonamide
519173-96-7P
519173-97-8P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]-2-methylbenzenesulfonamide
519173-98-9P, Ethanesulfonic acid
N-[[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]amide
519173-99-0P, 3,5-Dimethylisoxazole-4-sulfonic acid
N-[[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]amide
519174-00-6P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide
519174-01-7P, (R)-N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide
519174-02-8P, (R)-N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide
519174-03-9P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]-4-methoxybenzenesulfonamide
519174-04-0P, 2-Chloro-N-[[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]benzenesulfonamide
519174-05-1P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]-2-fluorobenzenesulfonamide
519174-06-2P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]-4-methylbenzenesulfonamide
519174-07-3P, Propane-2-sulfonic acid [[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]amide
519174-08-4P,

Propane-1-sulfonic acid [[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]amide 519174-10-8P,
2-[4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-cyanoacetamide 519174-11-9P, N-[[4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-12-0P,
(R)-N-[[4-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-13-1P,
N-[[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-14-2P,
N-[[5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-15-3P,
N-[[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-16-4P,
N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]phenylmethanesulfonamide 519174-17-5P,
N-[3-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide 519174-18-6P
, (R)-N-[[5-Chloro-2-[2-[4-(4-chlorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-19-7P,
(R)-N-[[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-20-0P,
(R)-N-[[5-Chloro-2-[2-[2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-21-1P,
(R)-N-[[5-Bromo-2-[2-[2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-22-2P,
(R)-N-[[2-[2-[2-Ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxo-ethoxy]-5-methylphenyl]acetyl]methanesulfonamide 519174-23-3P,
(R)-N-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide 519174-24-4P,
N-[3-[2-[2-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]propionyl]methanesulfonamide 519174-25-5P 519174-26-6P,
(R)-N-[3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide 519174-27-7P
519174-28-8P, (R)-N-[3-[2-[2-[2-Ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]propionyl]methanesulfonamide 519174-29-9P,
[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylamino]acetic acid 519174-30-2P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid 519174-31-3P, 3-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]acrylic acid 519174-32-4P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid 519174-33-5P,
3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid 519174-34-6P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-[(ethylamino)carbonyl]benzenesulfonamide 519174-35-7P,
5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-[(phenylamino)carbonyl]benzenesulfonamide 519174-36-8P,
5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-[(2-methylphenylamino)carbonyl]benzenesulfonamide 519174-37-9P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-[(4-fluorophenylamino)carbonyl]benzenesulfonamide 519174-38-0P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-(methoxycarbonyl)benzenesulfonamide 519174-39-1P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-(ethoxycarbonyl)benzenesulfonamide 519174-40-4P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-isobutyrylbenzenesulfonamide 519174-41-5P, 5-Chloro-N-(cyclopropylcarbonyl)-2-[2-[4-(4-fluorobenzyl)-

(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonamide
519174-42-6P 519174-43-7P 519174-44-8P, [[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]sulfonyl]amino]-oxoacetic acid 519174-45-9P
519174-47-1P, (R)-N-Acetyl-1-[5-chloro-2-[2-[4-(3,4-difluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide
519174-48-2P, (R)-N-Acetyl-1-[5-chloro-2-[2-[4-(4-chlorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide
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(R)-[5-Chloro-2-[2-[4-(4-chlorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-52-8P, 1-[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(cyclopropylcarbonyl)methanesulfonamide 519174-53-9P,
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519174-58-4P, N-Acetyl-1-[5-chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide
519174-59-5P, N-Acetyl-1-[5-bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide
519174-60-8P, N-Acetyl-1-[5-bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide
519174-61-9P, N-Acetyl-1-[5-bromo-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide
519174-62-0P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(2,2-dimethylpropionyl)methanesulfonamide 519174-63-1P, [5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-64-2P, [5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-65-3P, N-Acetyl-1-[5-chloro-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-66-4P, 1-[5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(cyclopropylcarbonyl)methanesulfonamide 519174-67-5P 519174-68-6P
519174-69-7P, 1-[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(cyclopropylcarbonyl)methanesulfonamide 519174-70-0P,
[5-Bromo-2-[2-[4-(4-chlorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-71-1P, N-Acetyl-1-[5-bromo-2-[2-[4-(4-chlorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-72-2P, N-Acetyl-1-[5-bromo-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-73-3P, [5-Bromo-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-74-4P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamino]-oxoacetic acid 519174-75-5P,
1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-[(1-hydroxycyclopropyl)carbonyl]methanesulfonamide
519174-76-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamino]-oxoacetic acid 519174-77-7P,
1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-

oxoethoxy]phenyl]-N-(methoxyacetyl)methanesulfonamide 519174-78-8P,
 N-Acetyl-1-[2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]methanesulfonamide 519174-79-9P,
 N-Acetyl-1-[2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]methanesulfonamide 519174-80-2P,
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 [2-[2-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]methanesulfonamide 519174-82-4P 519174-83-5P,
 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(3-hydroxy-3-methylbutyryl)methanesulfonamide 519174-84-6P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(2-hydroxy-2-methylpropionyl)methanesulfonamide 519174-85-7P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(hydroxyacetyl)methanesulfonamide 519174-86-8P 519174-87-9P 519174-88-0P, 1-[5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(hydroxyacetyl)methanesulfonamide 519174-89-1P, 1-[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(hydroxyacetyl)methanesulfonamide 519174-90-4P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(3-hydroxy-3-methylbutyryl)methanesulfonamide 519174-91-5P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-[(1-hydroxycyclopropyl)carbonyl]methanesulfonamide 519174-92-6P, 1-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]-N-(hydroxyacetyl)methanesulfonamide 519174-93-7P, 1-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]-N-(2-hydroxy-2-methylpropionyl)methanesulfonamide 519174-94-8P, 1-[2-[2-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]-N-(2-hydroxy-2-methylpropionyl)methanesulfonamide 519174-95-9P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(methoxycarbonyl)methanesulfonamide
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-benzylpiperazine derivs. as chemokine receptor CCR1 antagonists useful as immunomodulatory agents)

IT 519172-84-0P, (4S)-4-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenoxy]-Pyrrolidine-1,2S-Dicarboxylic acid Di-tert-Butyl Ester

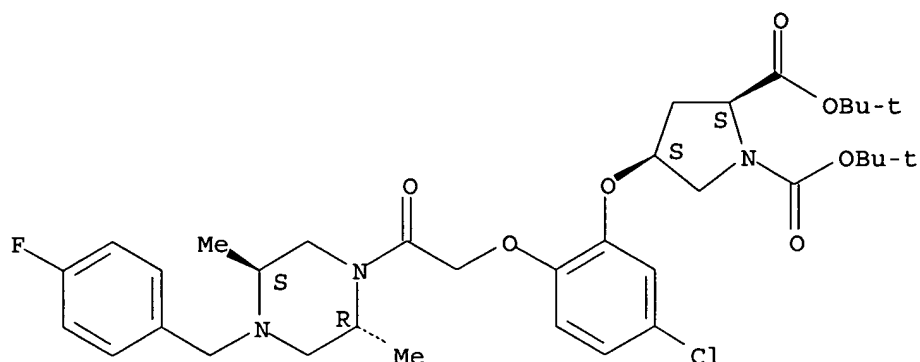
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of N-benzylpiperazine derivs. as chemokine receptor CCR1 antagonists useful as immunomodulatory agents)

RN 519172-84-0 CAPLUS

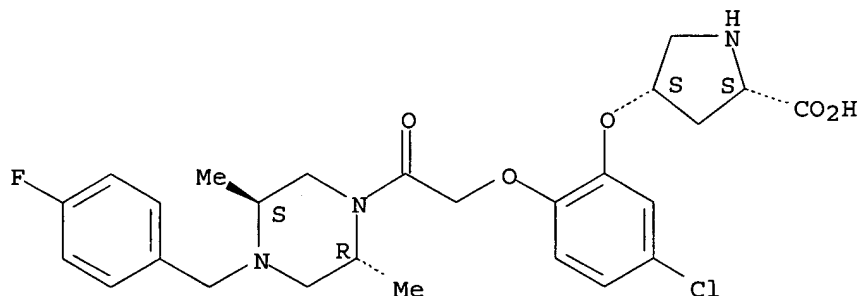
CN 1,2-Pyrrolidinedicarboxylic acid, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, bis(1,1-dimethylethyl) ester, (2S,4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **519172-85-1P**, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid dihydrochloride
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of N-benzylpiperazine derivs. as chemokine receptor CCR1 antagonists useful as immunomodulatory agents)
 RN 519172-85-1 CAPLUS
 CN L-Proline, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, dihydrochloride, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

IT **519172-86-2P**, (4S)-4-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenoxy]-1-Methyl-Pyrrolidine-(2S)-2-Carboxylic Acid dihydrochloride **519173-62-7P**, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-2-carboxylic acid **519173-65-0P**, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid **519173-67-2P**, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid **519173-69-4P**, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid

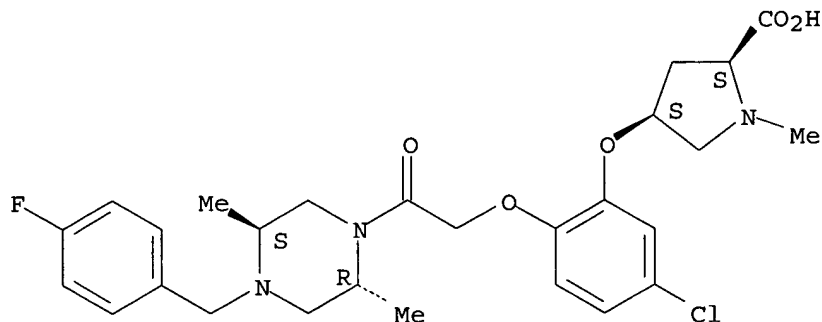
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-benzylpiperazine derivs. as chemokine receptor CCR1 antagonists useful as immunomodulatory agents)

RN 519172-86-2 CAPLUS

CN L-Proline, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-1-methyl-, dihydrochloride, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

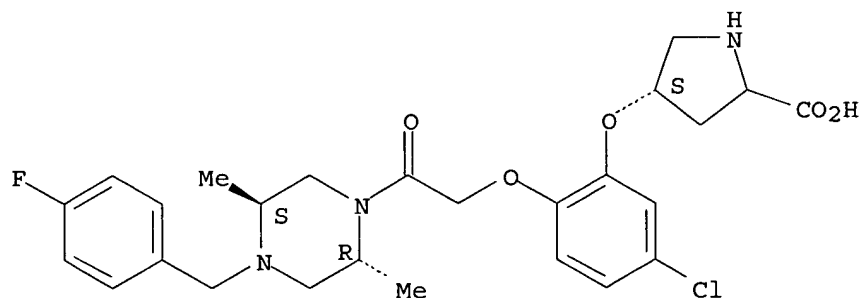


● 2 HCl

RN 519173-62-7 CAPLUS

CN Proline, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, (4S)- (9CI) (CA INDEX NAME)

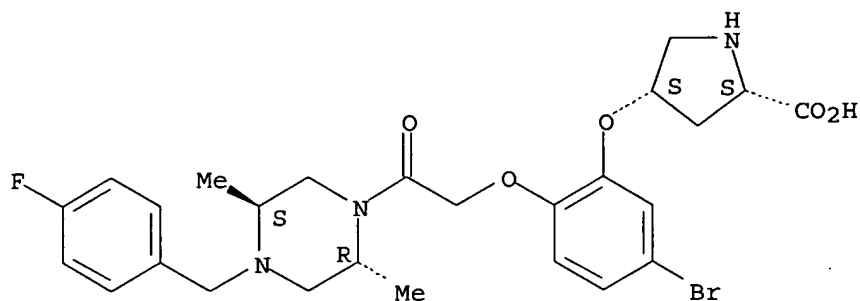
Absolute stereochemistry.



RN 519173-65-0 CAPLUS

CN L-Proline, 4-[5-bromo-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, (4S)- (9CI) (CA INDEX NAME)

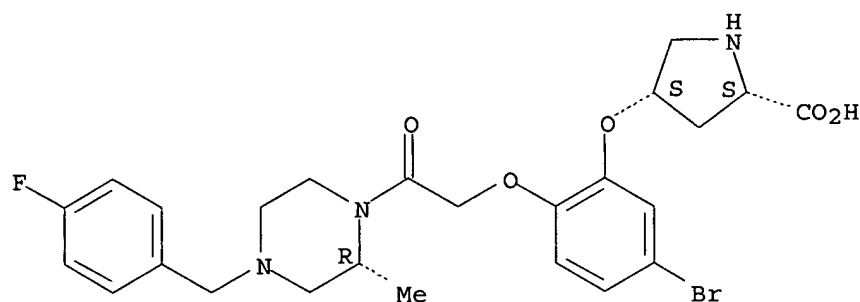
Absolute stereochemistry.



RN 519173-67-2 CAPLUS

CN L-Proline, 4-[5-bromo-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, (4S)- (9CI) (CA INDEX NAME)

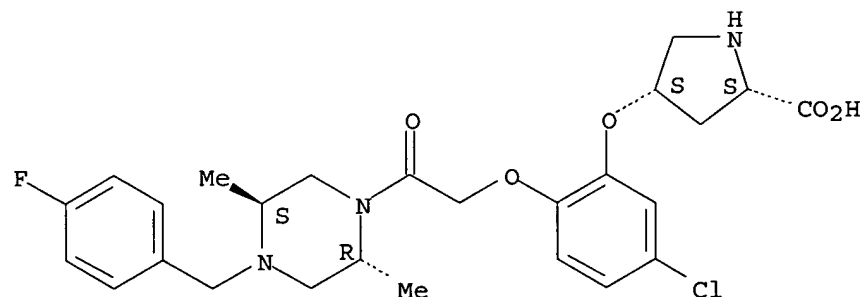
Absolute stereochemistry.



RN 519173-69-4 CAPLUS

CN L-Proline, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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ACCESSION NUMBER: 2004:387265 CAPLUS

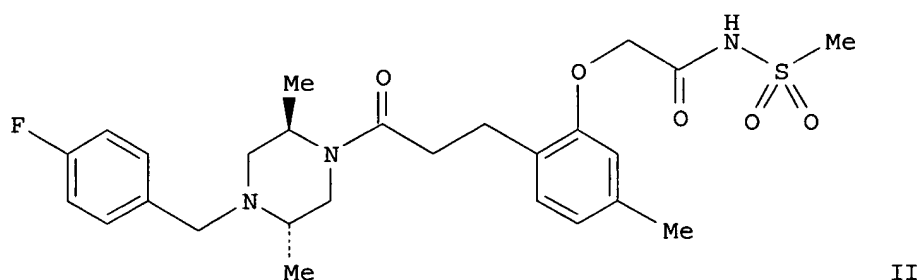
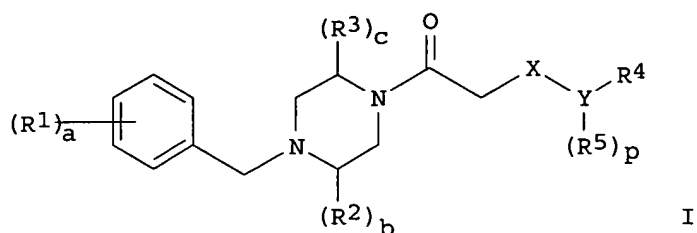
DOCUMENT NUMBER: 140:391297

TITLE: Preparation of piperazine derivatives as CCR1 antagonists

INVENTOR(S): Blumberg, Laura Cook; Brown, Matthew Frank; Gaweco,

Anderson See; Gladue, Ronald Paul; Hayward, Matthew
Merrill; Lundquist, Gregory Dean; Poss, Christopher
Stanley; Shavnya, Andre
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039376	A1	20040513	WO 2003-IB4612	20031020
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2498261	AA	20040513	CA 2003-2498261	20031020
AU 2003269364	A1	20040525	AU 2003-269364	20031020
BR 2003015777	A	20050913	BR 2003-15777	20031020
EP 1583533	A1	20051012	EP 2003-751145	20031020
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006506391	T2	20060223	JP 2004-547876	20031020
PRIORITY APPLN. INFO.:			US 2002-422590P	P 20021030
			WO 2003-IB4612	W 20031020
OTHER SOURCE(S):			MARPAT 140:391297	
GI				



AB Title compds. I [a = 0-5; b,c = 0-2; p = 0-4; X = O, S, CH₂, (un)substituted amino; Y = (hetero)aryl; R₁ = H, OH, halo, alkyl, alkoxy, etc.; R₂-3 = H, oxo, (cyclo)alkyl, aryl, etc.; R₄ = alkyl, etc.; R₅ = H, OH, halo, CN, etc.] are prepared For instance, (2R,5S)-1-(4-fluorobenzyl)-2,5-dimethylpiperazine (preparation given) is reacted with 7-methylchroman-2-one (PhMe, reflux 48 h), the resulting propanone treated with bromoacetic acid Me ester (THF, NaH) and the ester saponified to give II. All example compds. have IC₅₀ < 10 μM in the chemotaxis assay. I are useful for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal.

IC ICM A61K031-495

ICS A61P037-02

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 519171-77-8P 519171-85-8P, (2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid
519171-92-7P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenylsulfamoyl]acetic acid
519171-93-8P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylamino]propionic acid
hydrochloride 519171-96-1P 519171-98-3P, (2-Methylbenzenesulfonyl)carbamic acid 5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl ester
519171-99-4P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylsulfamoyl]propionic acid
519172-04-4P 519172-06-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylideneaminoxy]acetic acid
519172-07-7P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide
519172-09-9P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]sulfamide

519172-10-2P, N-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide
519172-14-6P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid 519172-16-8P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonyl]amino]acetic acid hydrochloride 519172-21-5P, 5-Chloro-N-(2,2-dimethylpropionyl)-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonamide 519172-22-6P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-(2-hydroxy-2-methylpropionyl)benzenesulfonamide
519172-30-6P 519172-32-8P 519172-33-9P, N-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]succinamic acid 519172-37-3P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]acetyl]methanesulfonamide 519172-45-3P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]propionic acid 519172-49-7P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethyl]amino]pyridine-3-carbonyl]amino]acetic acid 519172-55-5P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenylsulfanyl]-2-methylpropionic acid 519172-59-9P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonyl]-2-methylpropionic acid 519172-62-4P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenylmethanesulfonyl]acetic acid 519172-65-7P, N-[3-[3-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-6-methylpyridin-2-yl]propionyl]methanesulfonamide
519172-70-4P, 2-Amino-3-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionic acid 519172-73-7P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]methylamino]acetic acid 519172-75-9P, 2-[4-Chloro-2-(2H-tetrazol-5-ylmethoxy)phenoxy]-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 519172-77-1P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]nicotinic acid hydrochloride 519172-78-2P, [2-[2-[(2R)-2-Carbamoylmethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]-5-chlorophenoxy]acetic acid **519172-86-2P**, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-1-methylpyrrolidine-(2S)-2-carboxylic acid dihydrochloride 519172-87-3P 519172-88-4P, 6-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]nicotinic acid 519172-90-8P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-5-oxopentanoic acid 519172-94-2P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]dihydrofuran-2-one 519173-10-5P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-2-(1H-tetrazol-5-yl)ethanone hydrochloride 519173-13-8P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-3-(1H-tetrazol-5-yl)propan-1-one hydrochloride 519173-14-9P 519173-15-0P, N-[[2-[3-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methoxyphenoxy]acetyl]methanesulfonamide 519173-16-1P, [5-Chloro-2-[3-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]phenoxy]acetic acid 519173-17-2P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]oxoacetic acid 519173-18-3P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-19-4P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-20-7P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-

oxoethoxy]phenoxy]acetic acid 519173-21-8P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-22-9P, [5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-23-0P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-24-1P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-25-2P, N-[[5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-26-3P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-27-4P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-28-5P, 6-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyridine-2-carboxylic acid 519173-29-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-30-9P, (2R)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-31-0P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-32-1P, (R)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butanoic acid 519173-33-2P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-34-3P, (2S)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-35-4P, 2-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-36-5P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-37-6P, 2-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-38-7P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-39-8P, (2S)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-40-1P, (2S)-2-Amino-4-[5-bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-41-2P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyridine-2-carboxylic acid 519173-42-3P, N-[(2R)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyryl]methanesulfonamide 519173-43-4P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]thiazole-4-carboxylic acid 519173-44-5P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]furan-2-carboxylic acid 519173-45-6P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]furan-2-carboxylic acid 519173-46-7P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]thiophene-2-carboxylic acid 519173-47-8P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]furan-3-carboxylic acid 519173-48-9P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]thiophene-2-carboxylic acid 519173-49-0P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]furan-2-carboxylic acid 519173-50-3P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]furan-2-carboxylic acid 519173-51-4P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-5-(2-methoxyethyl)pyrimidine-2,4,6-trione

519173-53-6P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-5-methylpyrimidine-2,4,6-trione 519173-55-8P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-5-ethylpyrimidine-2,4,6-trione 519173-58-1P, (2R)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid 519173-60-5P, (2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid 519173-62-7P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-2-carboxylic acid 519173-63-8P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2,2-dimethylpropionic acid 519173-65-0P, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-67-2P, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-69-4P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-70-7P, N-[(4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxyl]methanesulfonamide 519173-72-9P 519173-73-0P 519173-74-1P 519173-75-2P 519173-76-3P 519173-77-4P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylsulfamoyl]acetic acid 519173-78-5P 519173-79-6P 519173-80-9P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylideneaminoxy]acetic acid 519173-81-0P, [1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ethylideneaminoxy]acetic acid 519173-82-1P, [1-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ethylideneaminoxy]acetic acid 519173-83-2P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]phenylmethyleaminoxy]acetic acid 519173-84-3P, [2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-methylbenzylideneaminoxy]acetic acid 519173-85-4P, (2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]propionic acid 519173-86-5P, (2R)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]propionic acid 519173-87-6P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]-2-methylpropionic acid 519173-88-7P, Methylsulfonylcarbamic acid 5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl ester 519173-89-8P 519173-90-1P, N-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]benzoyl]methanesulfonamide 519173-91-2P 519173-92-3P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519173-93-4P 519173-94-5P 519173-95-6P 519173-96-7P 519173-97-8P 519173-98-9P 519173-99-0P 519174-00-6P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-01-7P, (R)-N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-02-8P, (R)-N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-03-9P 519174-04-0P 519174-05-1P 519174-06-2P 519174-07-3P, Propane-2-sulfonic acid [[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]amide 519174-08-4P 519174-11-9P 519174-12-0P, (R)-N-[[4-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-13-1P 519174-14-2P 519174-15-3P 519174-16-4P 519174-17-5P 519174-18-6P,

(R) -N- [[5-Chloro-2-[2-[4-(4-chlorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-19-7P,
(R) -N- [[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-20-0P,
(R) -N- [[5-Chloro-2-[2-[2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-21-1P,
(R) -N- [[5-Bromo-2-[2-[2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-22-2P,
(R) -N- [[2-[2-[2-Ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]acetyl]methanesulfonamide 519174-23-3P,
(R) -N- [3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide 519174-24-4P,
N- [3-[2-[2-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]propionyl]methanesulfonamide 519174-25-5P 519174-26-6P,
(R) -N- [3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide 519174-27-7P
519174-28-8P, (R) -N- [3-[2-[2-[2-Ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]propionyl]methanesulfonamide 519174-29-9P,
[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylamino]acetic acid 519174-30-2P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid 519174-31-3P, 3-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]acrylic acid 519174-32-4P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid 519174-33-5P,
3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid 519174-34-6P 519174-35-7P 519174-36-8P
519174-37-9P 519174-38-0P 519174-39-1P 519174-40-4P 519174-41-5P
519174-42-6P 519174-43-7P 519174-44-8P 519174-45-9P 519174-52-8P,
(R) - [5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl] -N- ((cyclopropane) carbonyl) methanesulfonamide
519174-53-9P, (R) - [5-Chloro-2-[2-[4-(4-chlorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl] -N- (trifluoroacetyl) methanesulfonamide
519174-62-0P 519174-63-1P, [5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl] methanesulfonamide
519174-66-4P 519174-67-5P 519174-69-7P 519174-70-0P,
[5-Bromo-2-[2-[4-(4-chlorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl] methanesulfonamide 519174-73-3P, [5-Bromo-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl] methanesulfonamide 519174-74-4P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl] methanesulfonylamino] oxoacetic acid 519174-75-5P
519174-76-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl] methanesulfonylamino] oxoacetic acid 519174-77-7P
519174-78-8P, (R) -N-Acetyl [2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl] methanesulfonamide 519174-79-9P
519174-80-2P, [2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl] methanesulfonamide
519174-81-3P, [2-[2-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl] methanesulfonamide 519174-82-4P
519174-83-5P 519174-84-6P, (R) - [5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl] -N- (2-hydroxy-2-methylpropionyl) methanesulfonamide 519174-85-7P, (R) - [5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl] -N- (hydroxyacetyl) methanesulfonamide 519174-86-8P 519174-87-9P
519174-88-0P 519174-89-1P 519174-90-4P, (R) - [5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl] -N- (3-hydroxy-3-methylbutyryl) methanesulfonamide 519174-91-5P, (R) - [5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl] -N- ((1-hydroxycyclopropane) carbonyl) methanesulfonamide 519174-92-6P

519174-93-7P 519174-94-8P, (R)-[2-[2-[4-(4-Fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]-N-(2-hydroxy-2-methylpropionyl)methanesulfonamide 519174-95-9P, (R)-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(methoxycarbonyl)methanesulfonamide 519174-96-0P 519174-97-1P
519174-98-2P, N-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]-2,2-dimethylsuccinamic acid
519174-99-3P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridine-3-carbonyl]amino]acetic acid
519175-00-9P, N-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]succinamic acid
519175-01-0P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]acrylic acid
519175-02-1P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethylamino]pyridin-3-yl]propionic acid
519175-03-2P, N-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]propionyl]methanesulfonamide 519175-04-3P
2-Amino-3-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]propionic acid 519175-05-4P,
[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-ylmethyl]amino]acetic acid 519175-06-5P,
2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-6-methylpyrimidine-4-carboxylic acid 519175-07-6P,
2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-4-methylthiazole-5-carboxylic acid 519175-08-7P,
6-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]nicotinic acid 519175-09-8P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]nicotinic acid 519175-10-1P,
6-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-ylamino]methyl]nicotinic acid 519175-11-2P,
2-[4-Chloro-2-(2H-tetrazol-5-yloxy)phenoxy]-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 519175-12-3P, 2-[4-Bromo-2-(2H-tetrazol-5-yloxy)phenoxy]-1-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]ethanone 519175-13-4P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid 519175-14-5P,
[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid 519175-15-6P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid 519175-16-7P, [2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-4-methoxyphenyl]acetic acid 519175-17-8P,
3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionic acid 519175-18-9P, [4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid 519175-19-0P, [4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid 519175-20-3P, 3-[2-[2-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]propionic acid 519175-21-4P,
3-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]propionic acid 519175-22-5P,
3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionic acid 519175-23-6P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionic acid 519175-24-7P, [5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid 519175-25-8P, [5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid 519175-26-9P, [5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid

519175-27-0P, [5-Bromo-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid 519175-28-1P, [5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid 519175-29-2P, [5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid 519175-30-5P, [2-[2-[(2R)-2-Ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]acetic acid 519175-31-6P, [2-[2-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]acetic acid 519175-32-7P, [2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]acetic acid 519175-33-8P, 3-[2-[2-[(2R)-2-Ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]propionic acid 519175-35-0P, (R)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-4-oxobutanoic acid 519175-37-2P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-4-hydroxybut-3-enoic acid 519175-38-3P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]but-3-enoic acid 688031-91-6P 688031-92-7P 688031-94-9P, (R)-3-[N'-(5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl)ureido]propionic acid hydrochloride 688031-96-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted N-acylpiperazine derivs. as CCR1 antagonists)

IT 7035-10-1P, (5-Chloro-2-methoxyphenyl)methanol 7035-11-2P, 4-Chloro-2-chloromethyl-1-methoxybenzene 7048-38-6P, (5-Chloro-2-methoxyphenyl)acetonitrile 7569-62-2P, (5-Chloro-2-methoxyphenyl)acetic acid 24161-38-4P, (5-Chloro-2-hydroxyphenyl)acetic acid 25032-64-8P, 4-Chlorobut-3-enenitrile 27130-43-4P, 4-Chlorobut-2-enenitrile 56913-08-7P, (4-Chloro-2-methoxyphenoxy)acetic acid 62903-23-5P, 4-(5-Chloro-2-hydroxyphenyl)-4-oxobutanoic acid 66497-42-5P, 3-Hydroxy-6-methylpyridine-2-carboxaldehyde 76322-41-3P, (5-Chloro-2-hydroxyphenyl)acetic acid ethyl ester 82020-51-7P, 5-Chloro-2-methoxybenzenesulfonamide 82020-64-2P, 5-Chloro-2-hydroxybenzenesulfonamide 100119-68-4P, 4-(5-Chloro-2-hydroxyphenyl)-4-oxobutanoic acid ethyl ester 131803-48-0P, 6-Bromomethylnicotinic acid methyl ester 176433-49-1P, 2,5-Dichloropyridine-3-carboxaldehyde 217645-80-2P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzaldehyde 217648-11-8P, 2-Chloro-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 329219-99-0P, 7-Chlorobenzo-1,4-dioxin-2-one 331729-64-7P, 2-(5-Chloro-2-hydroxybenzyl)isindole-1,3-dione 364066-89-7P, (S)-2-(4-Fluorobenzylamino)propionic acid methyl ester 364066-90-0P, (2S)-2-[(2R)-2-((tert-Butoxycarbonyl)amino)propionyl](4-fluorobenzyl)amino]propionic acid methyl ester 364066-91-1P, (3R,6S)-1-(4-Fluorobenzyl)-3,6-dimethylpiperazine-2,5-dione 364066-97-7P, 2-(4-Chloro-2-nitrophenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 364066-98-8P, 2-(2-Amino-4-chlorophenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 364067-02-7P, 2-(2-Aminomethyl-4-chlorophenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 422270-29-9P, (R)-1-(4-Fluorobenzyl)-3-methylpiperazine 422270-30-2P, 2-Chloro-1-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]ethanone 422270-31-3P, 2-(4-Chloro-2-nitrophenoxy)-1-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]ethanone 422270-32-4P, 2-(2-Amino-4-chlorophenoxy)-1-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]ethanone 478833-41-9P, (2R,5S)-1-(4-Fluorobenzyl)-2,5-dimethylpiperazine 478833-49-7P, 2-(4-Chloro-2-hydroxymethylphenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 478833-52-2P, 2-(4-Chloro-2-chloromethylphenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-

yl]ethanone 478833-90-8P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid ethyl ester 519171-78-9P, 1-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-(2-hydroxy-4-methylphenyl)propan-1-one 519171-79-0P 519171-82-5P, 2-(4-Chloro-2-hydroxyphenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 519171-83-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid methyl ester 519171-88-1P 519171-90-5P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]carbamic acid 4-nitrophenyl ester 519171-91-6P, (R)-3-[N'-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid methyl ester 519171-94-9P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylamino]propionic acid methyl ester 519171-97-2P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]isoindole-1,3-dione 519172-01-1P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]acetic acid tert-butyl ester 519172-02-2P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]acetic acid hydrochloride 519172-08-8P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid 519172-11-3P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid ethyl ester 519172-12-4P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionic acid ethyl ester 519172-13-5P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionic acid 519172-17-9P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonamide 519172-18-0P 519172-19-1P 519172-23-7P, Acetic acid 2-[[[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzene]sulfonyl]amino]-1,1-dimethyl-2-oxoethyl ester 519172-25-9P, Thioacetic acid S-(5-chloro-2-methoxybenzyl) ester 519172-26-0P, (5-Chloro-2-methoxyphenyl)methanesulfonic acid 519172-27-1P, (5-Chloro-2-methoxyphenyl)methanesulfonamide 519172-28-2P, (5-Chloro-2-hydroxyphenyl)methanesulfonamide 519172-29-3P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519172-31-7P, Acetic acid 2-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenylmethanesulfonyl]amino]-1,1-dimethyl-2-oxoethyl ester 519172-34-0P, 1-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-hydroxyethanone 519172-35-1P, (R)-2-(5-Chloro-3-nitropyridin-2-yloxy)-1-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]ethanone 519172-36-2P, (R)-2-(3-Amino-5-chloropyridin-2-yloxy)-1-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]ethanone 519172-39-5P, (2,5-Dichloropyridin-3-yl)acetic acid methyl ester 519172-41-9P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]acetic acid methyl ester 519172-43-1P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]acetic acid 519172-46-4P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridine-3-carboxaldehyde 519172-47-5P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]acrylic acid ethyl ester 519172-48-6P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]propionic acid ethyl ester 519172-50-0P, [2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethyl]carbamic acid tert-butyl ester 519172-51-1P, 2-Amino-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 519172-52-2P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-

dimethylpiperazin-1-yl]-2-oxoethylamino]nicotinic acid methyl ester
 519172-53-3P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethylamino]nicotinic acid hydrochloride
 519172-54-4P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethylamino]pyridine-3-carbonyl]amino]acetic
 acid methyl ester 519172-56-6P, 6-Chloro-3,3-dimethylbenzo[1,4]oxathiin-
 2-one 519172-58-8P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethoxy]phenylsulfanyl]-2-methylpropionic acid
 ethyl ester 519172-60-2P 519172-61-3P 519172-63-5P,
 [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-
 oxoethoxy]benzylsulfanyl]acetic acid methyl ester 519172-66-8P,
 3-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-
 6-methylpyridine-2-carboxaldehyde 519172-67-9P, 3-[3-[2-[4-(4-
 Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-6-
 methylpyridin-2-yl]acrylic acid ethyl ester 519172-68-0P,
 3-[3-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-
 oxoethoxy]-6-methylpyridin-2-yl]propionic acid ethyl ester 519172-69-1P
 519172-71-5P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-2-nitropropionic acid ethyl
 ester 519172-72-6P, 2-Amino-3-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-
 2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionic acid ethyl ester
 519172-74-8P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]methylamino]acetic acid methyl
 ester 519172-76-0P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetonitrile 519172-79-3P,
 [2-(4-Fluorobenzylamino)ethyl]carbamic acid tert-butyl ester
 519172-80-6P, 4-[(2-tert-Butoxycarbonylaminoethyl)(4-
 fluorobenzyl)amino]but-2-enoic acid methyl ester 519172-81-7P,
 (R)-[4-(4-Fluorobenzyl)piperazin-2-yl]acetic acid methyl ester
 519172-82-8P 519172-83-9P, [2-[2-[(2R)-2-Carbamoylmethyl-4-(4-
 fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]-5-chlorophenoxy]acetic acid
 tert-butyl ester **519172-84-0P**, (4S)-4-[5-Chloro-2-[2-[4-(4-
 fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-
 oxoethoxy]phenoxy]pyrrolidine-1,2S-dicarboxylic acid di-tert-butyl ester
519172-85-1P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic
 acid dihydrochloride 519172-89-5P, 6-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-
 (2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]nicotinic
 acid methyl ester 519172-91-9P, 5-(5-Chloro-2-hydroxyphenyl)-5-
 oxopentanoic acid ethyl ester 519172-93-1P, 5-[5-Chloro-2-[2-[4-(4-
 fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-5-
 oxopentanoic acid ethyl ester 519172-98-6P, 2-(5-Chloro-3-nitropyridin-2-
 yloxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone
 519172-99-7P, 2-(3-Amino-5-chloropyridin-2-yloxy)-1-[4-(4-fluorobenzyl)-
 (2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 519173-00-3P,
 4-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-
 2-oxoethoxy]pyridin-3-yl]amino]butyric acid ethyl ester 519173-01-4P,
 [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-
 oxoethoxy]pyridin-3-ylamino]acetic acid ethyl ester 519173-04-7P,
 2-(4-Chloro-2-hydroxyphenoxy)-1-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-
 1-yl]ethanone 519173-08-1P, 2-(4-Chloro-2-isoxazol-5-ylphenoxy)-1-[4-(4-
 fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 519173-09-2P,
 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-
 oxoethoxy]phenyl]-3-oxopropionitrile 519173-11-6P, 4-(5-Chloro-2-
 hydroxyphenyl)-4-oxobutyronitrile 519173-12-7P, 4-[5-Chloro-2-[2-[4-(4-
 fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-4-
 oxobutyronitrile 688031-93-8P 688031-95-0P 688031-97-2P
 688031-99-4P 688032-00-0P 688032-04-4P, (R)-2-(4-Chloro-2-
 cyanophenoxy)-1-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]ethanone
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation of substituted N-acylpiperazine derivs. as CCR1 antagonists)

IT 519172-86-2P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-1-methylpyrrolidine-(2S)-2-carboxylic acid dihydrochloride 519173-62-7P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-2-carboxylic acid 519173-65-0P, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-67-2P, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-69-4P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid

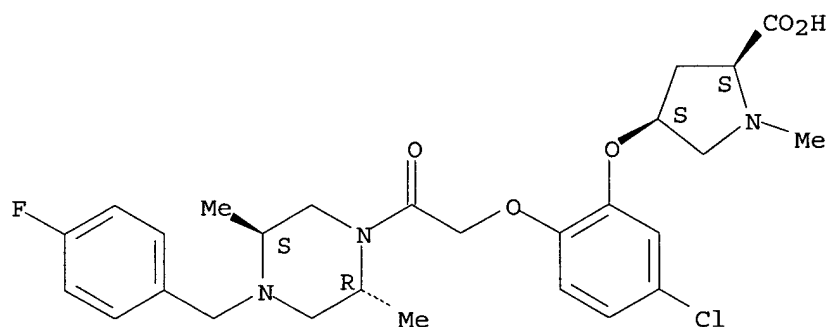
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted N-acylpiperazine derivs. as CCR1 antagonists)

RN 519172-86-2 CAPLUS

CN L-Proline, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-1-methyl-, dihydrochloride, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

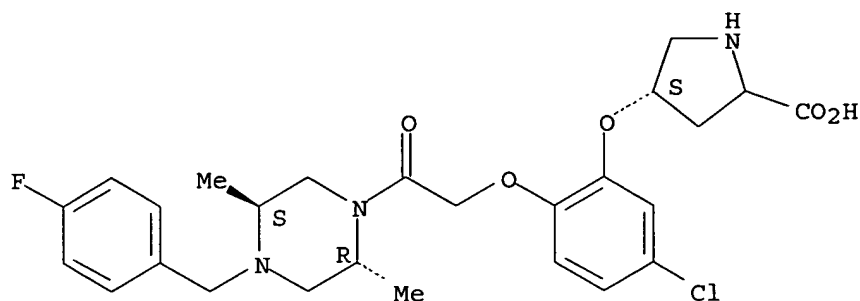


● 2 HCl

RN 519173-62-7 CAPLUS

CN Proline, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, (4S)- (9CI) (CA INDEX NAME)

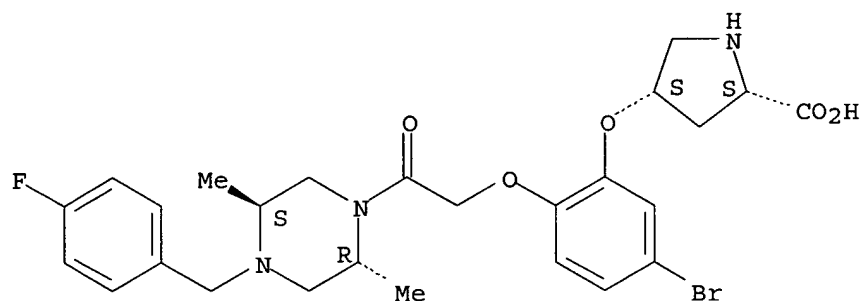
Absolute stereochemistry.



RN 519173-65-0 CAPLUS

CN L-Proline, 4-[5-bromo-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, (4S)- (9CI) (CA INDEX NAME)

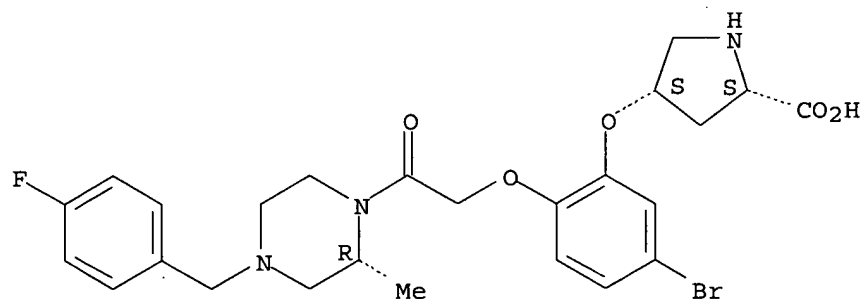
Absolute stereochemistry.



RN 519173-67-2 CAPLUS

CN L-Proline, 4-[5-bromo-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, (4S)- (9CI) (CA INDEX NAME)

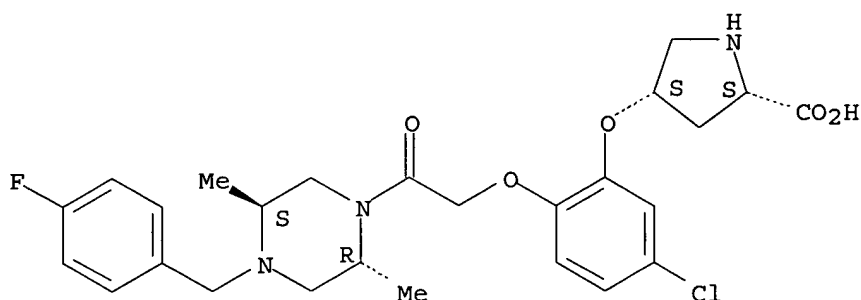
Absolute stereochemistry.



RN 519173-69-4 CAPLUS

CN L-Proline, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



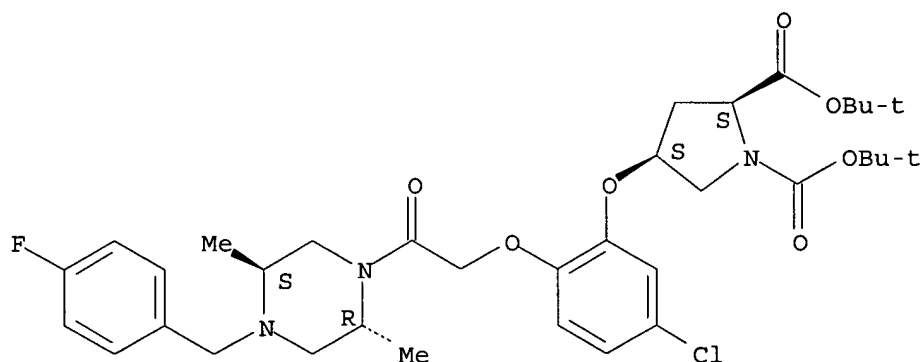
IT 519172-84-0P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-1,2S-dicarboxylic acid di-tert-butyl ester 519172-85-1P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid dihydrochloride
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted N-acylpiperazine derivs. as CCR1 antagonists)

RN 519172-84-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, bis(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

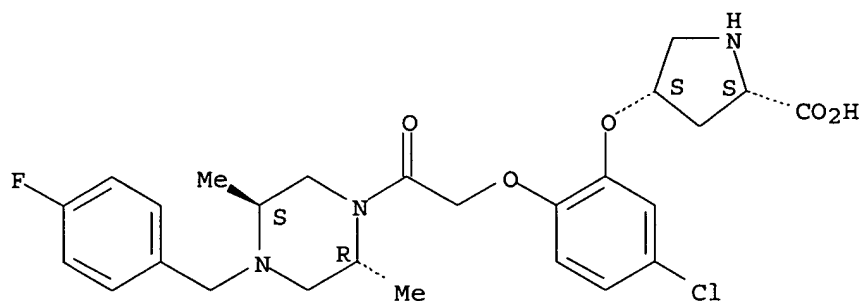
Absolute stereochemistry.



RN 519172-85-1 CAPLUS

CN L-Proline, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, dihydrochloride, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L47 ANSWER 11 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:347646 CAPLUS

DOCUMENT NUMBER: 141:89330

TITLE: A simple acromelic acid analog potentially useful for receptor photoaffinity labeling and biochemical studies

AUTHOR(S): Furuta, Kyoji; Wang, Guang Xing; Minami, Toshiaki; Nishizawa, Mikio; Ito, Seiji; Suzuki, Masaaki

CORPORATE SOURCE: Graduate School of Medicine, Regeneration and Advanced Medical Science, Gifu University, Gifu, 501-1193, Japan

SOURCE: Tetrahedron Letters (2004), 45(20), 3933-3936

CODEN: TELEAY; ISSN: 0040-4039

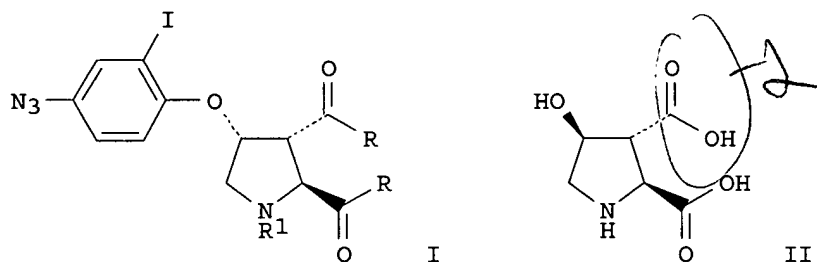
PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:89330

GI



AB A novel acromelic acid analog possessing an azido-functionalized Ph group, I (R = OH, R₁ = H), was designed and synthesized as a biochem. probe for studies on kainoid receptors. Thus, 4-hydroxyproline derivative II was converted to the di-Me ester which was coupled with 4-azido-2-iodophenol to give I (R = MeO, R₁ = Boc) which was deprotected and hydrolyzed to give the diacid. The analog exerted a biol. activity equivalent to natural acromelic acid A, suggesting that both compds. possibly bind to the same target biomol. In order to utilize the probe in photoaffinity labeling expts., a procedure for the introduction of radioactive iodine into the

mol. was established.

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 31

IT **714964-30-4P**

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);

BIOL (Biological study); PREP (Preparation)

(preparation of azidoiodophenyl acromelic acid analog as photoaffinity labeling probe tested in mech. allodynia induction)

IT 89487-91-2P, 2-Iodo-4-nitrophenol 125728-62-3P, 2-Iodo-4-azidophenol

375806-94-3P 714964-31-5P **714964-32-6P 714964-33-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of azidoiodophenyl acromelic acid analog as photoaffinity labeling probe tested in mech. allodynia induction)

IT **714964-30-4P**

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);

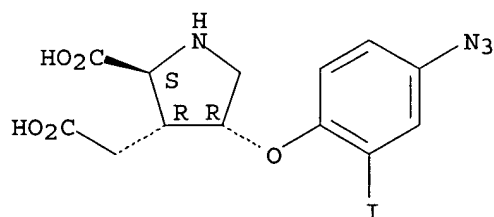
BIOL (Biological study); PREP (Preparation)

(preparation of azidoiodophenyl acromelic acid analog as photoaffinity labeling probe tested in mech. allodynia induction)

RN 714964-30-4 CAPLUS

CN 3-Pyrrolidineacetic acid, 4-(4-azido-2-iodophenoxy)-2-carboxy-, (2S,3R,4R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **714964-32-6P 714964-33-7P**

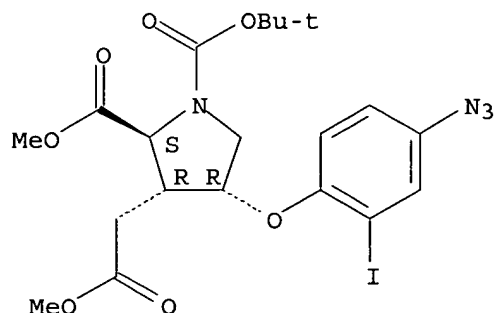
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of azidoiodophenyl acromelic acid analog as photoaffinity labeling probe tested in mech. allodynia induction)

RN 714964-32-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(4-azido-2-iodophenoxy)-3-(2-methoxy-2-oxoethyl)-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,3R,4R) - (9CI) (CA INDEX NAME)

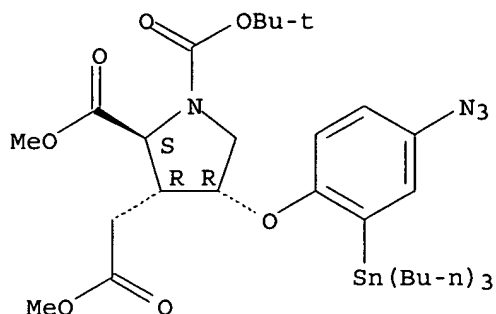
Absolute stereochemistry.



RN 714964-33-7 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[4-azido-2-(tributylstannyl)phenoxy]-3-(2-methoxy-2-oxoethyl)-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,3R,4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 12 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:60463 CAPLUS

DOCUMENT NUMBER: 140:111265

TITLE: Preparation of azetidinecarboxylic acid and pyrrolidinecarboxylic acid N-hydroxyamide derivatives as antibacterial agents

INVENTOR(S): Raju, Bore G.; Odowd, Hardwin; Gao, Hongwu; Patel, Dinesh V.; Trias, Joaquim

PATENT ASSIGNEE(S): Vicuron Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 172 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

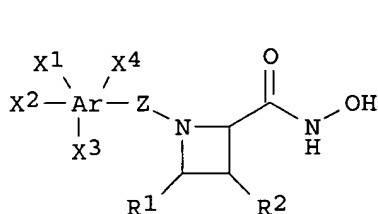
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

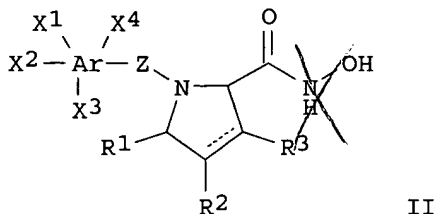
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007444	A2	20040122	WO 2003-US21838	20030711
WO 2004007444	A3	20040910		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2492035	AA	20040115	CA 2003-2492035	20030711
EP 1539744	A2	20050615	EP 2003-748939	20030711
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2005536510	T2	20051202	JP 2004-521744	20030711
PRIORITY APPLN. INFO.:			US 2002-394862P	20020711
			WO 2003-US21838	20030711

OTHER SOURCE(S) :
GI

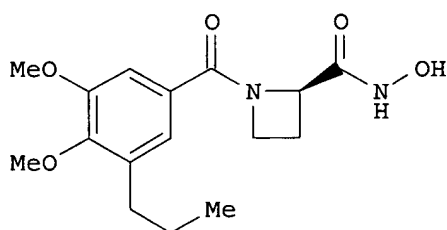
MARPAT 140:111265



I



II



III

AB Title compds. I or II [wherein A = (hetero)aryl; X1-X4 = independently H, (halo)alkyl, (halo)alkylthio, (halo)alkylsulfinyl, (halo)alkylsulfonyl, hydroxy(alkyl), alkoxy(alkyl), haloalkoxy, alkenyl, alkenyloxy(alkyl), alkynyl(oxy), NO₂, halo, cycloalkyl(alkyl), arylalkoxy(alkyl), haloarylalk(yn)yl, alkylsilylalkynyl, aryl, aminocarbonylalkyl, carboxylate, carboxy, carboxamido, or (un)substituted heterocyclyl; R1 and R3 = independently H, (halo)alkyl, hydroxyalkyl, alkenyl, alkynyl, cycloalkyl, halo, OH, alkoxy, or (un)substituted (hetero)aryl or aryloxy; R2 = H, (halo)alkyl, hydroxyalkyl, alkenyl, alkynyl, cycloalkyl, halo, OH, alkoxy, or (un)substituted (hetero)aryl or aryloxy; ; Z = CH₂ or CO; and pharmaceutically acceptable salts, tautomers, and prodrugs thereof] were prepared as inhibitors of UDP-3-O-(R-3-hydroxymyristoyl)-N-acetylglucosamine deacetylase (LpxC deacetylase), an enzyme present in gram neg. bacteria (no data). For example, azetidine-2R-carboxylic acid Me ester hydrochloride salt was coupled with 3,4-dimethoxy-5-propylbenzoic acid in DMF to give the benzoylazetidinyll derivative (81%). The ester was treated with aqueous hydroxylamine in dioxane to afford III. Preferred compds. of the invention have MIC ≤ 128 µg/mL against at least one of a specified list of bacteria (no data). Thus, I, II, and their pharmaceutical compns. are useful as antimicrobials and antibiotics (no data).

IC ICM C07D

CC 27-5 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 63

IT 4073-35-2P, 3,5-Dibromo-4-methoxybenzoic acid 5468-22-4P, 3,4-Dimethoxy-5-iodobenzoic acid 20731-48-0P, 3-Bromo-4,5-dimethoxybenzoic acid 22812-61-9P, 3,5-Dibromo-4-methoxybenzoic acid methyl ester 33185-56-7P, 1-Hydroxy-2-trifluoromethylthiobenzene 35750-24-4P, 4-Allyloxybenzoic acid methyl ester 50667-82-8P, 3,5-Bis(dimethylthiocarbamoyloxy)benzoic acid methyl ester 50930-21-7P, 3,5-Bis(dimethylcarbamoylethio)benzoic acid methyl ester 53596-60-4P, 3-Allyl-4-hydroxybenzoic acid methyl ester 71295-21-1P, 5-Bromo-2,3-dimethoxybenzaldehyde 71295-24-4P, 3-Butyl-4,5-

dimethoxybenzoic acid methyl ester 71295-25-5P, 3-Butyl-4,5-dimethoxybenzoic acid 82174-08-1P, (3-Trifluoromethylthiophenyl)methanol 82793-38-2P, 4-Methoxy-5-propylbenzoic acid 88489-62-7P, 3-[(1,2,2,2-Tetrafluoro-1-trifluoromethylethyl)thio]benzoic acid methyl ester 88489-75-2P, 3-[(1,2,2,2-Tetrafluoro-1-trifluoromethylethyl)thio]benzoic acid 99423-91-3P, 3,4-Dimethoxy-5-propylbenzyl alcohol 114676-59-4P, (2R,4R)-4-Hydroxypyrrolidine-2-carboxylic acid methyl ester hydrochloride 114676-69-6P 126224-84-8P, 1-(5-Bromo-2,3-dimethoxyphenyl)propan-1-ol 135042-17-0P 137421-52-4P, 4-Allyloxy-3-allylbenzoic acid methyl ester 137421-53-5P, 3,5-Diallyl-4-hydroxybenzoic acid methyl ester 155075-23-3P 171002-53-2P, 4-Allyloxy-3-methoxybenzoic acid methyl ester 188029-71-2P, (R)-2-[(Benzyloxy)carbamoyl]pyrrolidine-1-carboxylic acid tert-butyl ester 199484-24-7P, 3-Allyl-4,5-dimethoxybenzoic acid methyl ester 199484-25-8P, 4-Hydroxy-3-methoxy-5-propylbenzoic acid methyl ester 199484-26-9P, 3,4-Dimethoxy-5-propylbenzoic acid 199484-27-0P, 3,4-Dimethoxy-5-propylbenzoic acid methyl ester 220652-51-7P 228857-58-7P 256487-77-1P 261952-22-1P, 2-Trifluoromethoxyanisole 272130-65-1P, 3-Allyl-4-methoxybenzoic acid methyl ester 276697-76-8P, 1-Allyloxy-2-trifluoromethoxybenzene 361367-93-3P 436145-25-4P, 3,5-Dimercaptobenzoic acid methyl ester 436145-39-0P, 3-[(Dimethylthiocarbamoyl)oxy]-5-hydroxybenzoic acid methyl ester 445018-77-9P, 4-Methoxy-3-propyl-5-trifluoromethoxybenzoic acid 536746-99-3P, (2R,4R)-4-Hydroxy-1-tritylpyrrolidine-2-carboxylic acid methyl ester 647854-53-3P, 3-Allyl-4-hydroxy-5-methoxybenzoic acid methyl ester 647854-54-4P, (R)-2-[(Benzyloxy)carbamoyl]pyrrolidine hydrochloride 647854-55-5P 647854-57-7P, (R)-1-(3,4-Dimethoxy-5-propylbenzoyl)azetidine-2-carboxylic acid methyl ester 647854-59-9P, 3-Allyl-4-allyloxy-5-methoxybenzoic acid methyl ester 647854-60-2P, 3-Allyl-4-allyloxy-5-methoxybenzoic acid 647854-61-3P, 9-Methoxy-2,5-dihydrobenzo[b]oxepine-7-carboxylic acid 647854-62-4P, (R)-1-[(9-Methoxy-2,5-dihydrobenzo[b]oxepin-7-yl)carbonyl]azetidine-2-carboxylic acid methyl ester 647854-65-7P, (R)-1-(3-Allyl-4-allyloxy-5-methoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647854-67-9P, (R)-1-(3,4,5-Triethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647854-69-1P, (R)-1-(3,4,5-Trimethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647854-71-5P, Methanesulfonic acid 3,4-dimethoxy-5-propylbenzyl ester 647854-74-8P, (R)-1-(3,5-Dimethyl-4-nitrobenzoyl)azetidine-2-carboxylic acid methyl ester 647854-76-0P, (R)-1-(3,5-Dimethoxy-4-methylbenzoyl)azetidine-2-carboxylic acid methyl ester 647854-78-2P, 3-(3-Hydroxypropyl)-4,5-dimethoxybenzoic acid 647854-79-3P, (R)-1-[3-(3-Hydroxypropyl)-4,5-dimethoxybenzoyl]azetidine-2-carboxylic acid methyl ester 647854-81-7P, (R)-1-(3-Trifluoromethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647854-83-9P, (R)-1-(3,5-Dibromo-4-methylbenzoyl)azetidine-2-carboxylic acid methyl ester 647854-85-1P, (R)-1-(3-Methoxy-4-methylbenzoyl)azetidine-2-carboxylic acid methyl ester 647854-87-3P, (R)-1-(3,5-Dimethylbenzoyl)azetidine-2-carboxylic acid methyl ester 647854-89-5P, 4-Hydroxy-3-methoxy-5-propylbenzoic acid 647854-90-8P, (R)-1-(4-Hydroxy-3-methoxy-5-propylbenzoyl)azetidine-2-carboxylic acid methyl ester 647854-92-0P, 3-(3-Allyloxypropyl)-4,5-dimethoxybenzoic acid 647854-93-1P, (R)-1-[3-(3-Allyloxypropyl)-4,5-dimethoxybenzoyl]azetidine-2-carboxylic acid methyl ester 647854-95-3P, 3-[3-(Benzyloxy)propyl]-4,5-dimethoxybenzoic acid 647854-96-4P, (R)-1-[3-[3-(Benzyloxy)propyl]-4,5-dimethoxybenzoyl]azetidine-2-carboxylic acid methyl ester 647854-98-6P, 3,4-Dimethoxy-5-(3-propoxypropyl)benzoic acid 647854-99-7P, (R)-1-[3,4-Dimethoxy-5-(3-propoxypropyl)benzoyl]azetidine-2-carboxylic acid methyl ester 647855-01-4P, 3-Cyclopropylmethyl-4,5-dimethoxybenzoic acid methyl ester 647855-02-5P, 3-Cyclopropylmethyl-4,5-dimethoxybenzoic acid

647855-03-6P, (R)-1-(3-Cyclopropylmethyl-4,5-dimethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647855-05-8P, 3-(3-Hydroxypropyl)-4,5-dimethoxybenzoic acid methyl ester 647855-06-9P, 3,4-Dimethoxy-5-(3-oxopropyl)benzoic acid methyl ester 647855-07-0P, 3-(Hex-3-enyl)-4,5-dimethoxybenzoic acid methyl ester 647855-08-1P, 3-Hexyl-4,5-dimethoxybenzoic acid methyl ester 647855-09-2P, 3-Hexyl-4,5-dimethoxybenzoic acid 647855-10-5P, (R)-1-(3-Hexyl-4,5-dimethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647855-12-7P, 3,4-Dimethoxy-5-(pent-3-enyl)benzoic acid methyl ester 647855-13-8P, 3,4-Dimethoxy-5-pentylbenzoic acid methyl ester 647855-14-9P, 3,4-Dimethoxy-5-pentylbenzoic acid 647855-15-0P, (R)-1-(3,4-Dimethoxy-5-pentylbenzoyl)azetidine-2-carboxylic acid methyl ester 647855-18-3P, 4-Nitro-2-trifluoromethoxyanisole 647855-19-4P, 4-Amino-2-trifluoromethoxyanisole hydrochloride 647855-20-7P, 4-Iodo-2-trifluoromethoxyanisole 647855-22-9P, 4-Methoxy-3-trifluoromethoxybenzoic acid 647855-23-0P, (R)-1-(4-Methoxy-3-trifluoromethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647855-28-5P, 1-Allyloxy-4-nitro-2-trifluoromethoxybenzene 647855-29-6P, 4-Allyloxy-3-trifluoromethoxyaniline 647855-30-9P, 1-Allyloxy-4-iodo-2-trifluoromethoxybenzene 647855-31-0P, 4-Allyloxy-3-trifluoromethoxybenzoic acid 647855-32-1P, (R)-1-(4-Allyloxy-3-trifluoromethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647855-34-3P, (R)-2-[(Benzyloxy)carbamoyl]azetidine-1-carboxylic acid tert-butyl ester 647855-35-4P 647855-37-6P 647855-39-8P, 3,4-Dimethoxy-5-(3-methoxypropyl)benzoic acid 647855-40-1P 647855-42-3P, 3-(3-Ethoxypropyl)-4,5-dimethoxybenzoic acid 647855-43-4P 647855-45-6P, 3-Allyl-4,5-dimethoxybenzoic acid 647855-46-7P, (R)-1-(3-Allyl-4,5-dimethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647855-48-9P, 3-But-3-enyl-4,5-dimethoxybenzoic acid methyl ester 647855-49-0P, (R)-1-(3-Butyl-4,5-dimethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647855-51-4P, 5-Bromo-1,2-dimethoxy-3-(3,3,3-trifluoropropenyl)benzene 647855-52-5P, 3,4-Dimethoxy-5-(3,3,3-trifluoropropenyl)benzoic acid 647855-53-6P, 3,4-Dimethoxy-5-(3,3,3-trifluoropropyl)benzoic acid 647855-54-7P, (R)-1-[3,4-Dimethoxy-5-(3,3,3-trifluoropropyl)benzoyl]azetidine-2-carboxylic acid methyl ester 647855-56-9P, 3-[(Dimethylcarbamoyl)methyl]-4,5-dimethoxybenzoic acid methyl ester 647855-57-0P 647855-59-2P, (R)-1-(3,5-Dibromo-4-methoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647855-61-6P, (R)-1-(3-Iodo-4,5-dimethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647855-63-8P 647855-64-9P, 3-(3-Fluoropropyl)-4,5-dimethoxybenzoic acid methyl ester 647855-65-0P, (R)-1-[3-(3-Fluoropropyl)-4,5-dimethoxybenzoyl]azetidine-2-carboxylic acid methyl ester 647855-67-2P, (R)-1-(3-Trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester 647855-69-4P, (R)-1-(4-Trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester 647855-72-9P, 2-Allyl-4-nitro-6-trifluoromethoxyphenol 647855-73-0P, 1-Allyl-2-methoxy-5-nitro-3-trifluoromethoxybenzene 647855-74-1P, (4-Methoxy-3-propyl-5-trifluoromethoxyphenyl)amine hydrochloride 647855-75-2P, 5-Iodo-2-methoxy-1-propyl-3-trifluoromethoxybenzene 647855-76-3P, (R)-1-(4-Methoxy-3-propyl-5-trifluoromethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647855-78-5P, (R)-1-(3-Bromo-4,5-dimethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647855-80-9P, 3,4-Dimethoxy-5-(trimethylsilanylethynyl)benzoic acid 647855-81-0P, 3-Ethynyl-4,5-dimethoxybenzoic acid 647855-83-2P, 3,4-Dimethoxy-5-prop-1-ynylbenzoic acid 647855-85-4P, 3-Methoxy-5-propyl-4-(trifluoromethanesulfonyloxy)benzoic acid methyl ester 647855-86-5P, 3-Methoxy-5-propylbenzoic acid methyl ester 647855-88-7P, 3-[(Dimethylcarbamoyl)thio]-4-methoxybenzoic acid methyl ester 647855-89-8P, 3-Mercapto-4-methoxybenzoic acid methyl ester 647855-90-1P, 4-Methoxy-3-trifluoromethylthiobenzoic acid methyl ester

647855-92-3P, (R)-1-[3-[(1,2,2,2-Tetrafluoro-1-trifluoromethylethyl)thio]benzoyl]azetidine-2-carboxylic acid methyl ester
647855-94-5P, 3-[(Dimethylthiocarbamoyl)oxy]-5-methoxybenzoic acid methyl ester
647855-95-6P, 3-[(Dimethylcarbamoyl)thio]-5-methoxybenzoic acid methyl ester
647855-96-7P, 3-Mercapto-5-methoxybenzoic acid methyl ester
647855-97-8P, 3-Methoxy-5-trifluoromethylthiobenzoic acid methyl ester
647855-98-9P, 3-Methoxy-5-trifluoromethylthiobenzoic acid 647856-00-6P, 4-Methoxy-3-nitro-5-propylbenzoic acid methyl ester 647856-01-7P, 3-Amino-4-methoxy-5-propylbenzoic acid methyl ester 647856-02-8P, 2-(Ethoxythiocarbonylthio)-4-methoxy-5-propylbenzoic acid methyl ester 647856-03-9P, 3-Mercapto-4-methoxy-5-propylbenzoic acid methyl ester 647856-04-0P, 4-Methoxy-3-propyl-5-trifluoromethylthiobenzoic acid methyl ester 647856-05-1P, 4-Methoxy-3-propyl-5-trifluoromethylthiobenzoic acid 647856-06-2P, (R)-1-(4-Methoxy-3-propyl-5-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester 647856-08-4P, 5-Bromo-1-(1-fluoropropyl)-2,3-dimethoxybenzene 647856-10-8P, 4-Bromo-1-methylthio-2-trifluoromethoxybenzene 647856-12-0P, 3-(2,2,2-Trifluoroethylthio)benzoic acid methyl ester 647856-21-1P, 3-[(Dimethylthiocarbamoyl)oxy]-4,5-dimethoxybenzoic acid methyl ester 647856-22-2P, 3-[(Dimethylcarbamoyl)thio]-4,5-dimethoxybenzoic acid methyl ester 647856-23-3P, 3-Mercapto-4,5-dimethoxybenzoic acid methyl ester 647856-24-4P, 3,4-Dimethoxy-5-trifluoromethylthiobenzoic acid methyl ester 647856-25-5P, 3,4-Dimethoxy-5-trifluoromethylthiobenzoic acid 647856-26-6P, (R)-1-(3,4-Dimethoxy-5-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester 647856-28-8P, 4-Benzyloxy-1-bromo-2-trifluoromethoxybenzene 647856-29-9P, 4-Benzyloxy-3-trifluoromethoxybenzoic acid 647856-31-3P, (R)-1-(4-Benzyloxy-3-trifluoromethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647856-32-4P, (R)-1-(4-Hydroxy-3-trifluoromethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647856-33-5P, (R)-1-[4-(Trifluoromethanesulfonyloxy)-3-trifluoromethoxybenzoyl]azetidine-2-carboxylic acid methyl ester 647856-34-6P, (R)-1-(3-Trifluoromethoxy-4-vinylbenzoyl)azetidine-2-carboxylic acid methyl ester 647856-37-9P, (R)-1-(4-Ethyl-3-trifluoromethoxybenzoyl)azetidine-2-carboxylic acid methyl ester 647856-39-1P, 4-Bromo-1-hydroxy-2-trifluoromethylthiobenzene 647856-40-4P, 1-Benzyloxy-4-bromo-2-trifluoromethylthiobenzene 647856-41-5P, 4-Benzyloxy-3-trifluoromethylthiobenzoic acid 647856-42-6P, (R)-1-(4-Benzyloxy-3-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester 647856-44-8P, (R)-1-(4-Hydroxy-3-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester 647856-45-9P, (R)-1-[4-(Trifluoromethanesulfonyloxy)-3-trifluoromethylthiobenzoyl]azetidine-2-carboxylic acid methyl ester 647856-46-0P, (R)-1-(3-Trifluoromethylthio-4-vinylbenzoyl)azetidine-2-carboxylic acid methyl ester 647856-48-2P, (R)-1-(4-Ethyl-3-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester 647856-50-6P, (R)-1-(4-Allyl-3-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester 647856-52-8P, (R)-1-(4-Propyl-3-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester 647856-54-0P, 5,6-Dimethoxybiphenyl-3-carboxylic acid 647856-55-1P, (R)-1-[(5,6-Dimethoxybiphenyl-3-yl)carbonyl]azetidine-2-carboxylic acid methyl ester 647856-59-5P, (R)-1-[3-Trifluoromethylthio-4-(trimethylsilyl)ethynyl]benzoyl]azetidine-2-carboxylic acid methyl ester 647856-63-1P, (R)-1-(4-Ethynyl-3-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester 647856-66-4P, (R)-1-(4-Pent-1-ynyl-3-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester 647856-68-6P, (R)-1-(4-Pentyl-3-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester 647856-72-2P, (R)-1-[4-(Fluorophenylethynyl)-3-trifluoromethylthiobenzoyl]azetidine-2-carboxylic acid methyl ester 647856-74-4P, (R)-1-[4-[2-(3-Fluorophenyl)ethyl]-3-

trifluoromethylthiobenzoyl]azetidine-2-carboxylic acid methyl ester
 647856-77-7P, 3-[(3-Fluorophenyl)ethynyl]-4,5-dimethoxybenzoic acid
 647856-79-9P, (R)-1-[3-[(3-Fluorophenyl)ethynyl]-4,5-dimethoxybenzoyl]azetidine-2-carboxylic acid methyl ester 647856-83-5P,
 (R)-1-(4-Allyloxy-3-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid
 methyl ester 647856-86-8P, (R)-1-(4-Propoxy-3-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester
 647856-89-1P, (R)-1-[4-[(But-3-enyl)oxy]-3-trifluoromethylthiobenzoyl]azetidine-2-carboxylic acid methyl ester 647856-92-6P, (R)-1-(4-Butoxy-3-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester
 647856-96-0P, (R)-1-[4-(3-Methylbut-3-enyloxy)-3-trifluoromethylthiobenzoyl]azetidine-2-carboxylic acid methyl ester
 647856-98-2P, (R)-1-[4-[(Prop-2-ynyl)oxy]-3-trifluoromethylthiobenzoyl]azetidine-2-carboxylic acid methyl ester 647857-00-9P, (R)-1-(4-Ethoxy-3-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester
 647857-02-1P, (R)-1-[4-(2,2,2-Trifluoroethoxy)-3-trifluoromethylthiobenzoyl]azetidine-2-carboxylic acid methyl ester
 647857-04-3P, [Benzhydryl(2-oxobutyl)amino]acetic acid tert-butyl ester
 647857-05-4P, [Benzhydryl(2-hydroxybutyl)amino]acetic acid tert-butyl ester 647857-06-5P, [Benzhydryl(2-chlorobutyl)amino]acetic acid
 tert-butyl ester 647857-07-6P 647857-08-7P 647857-09-8P
 647857-10-1P 647857-11-2P 647857-13-4P, 4-Bromo-2-trifluoromethoxy-1-trifluoromethylthiobenzene 647857-14-5P, 3-Trifluoromethoxy-4-trifluoromethylthiobenzoyl]azetidine-2-carboxylic acid methyl ester
 647857-15-6P, (R)-1-(3-Trifluoromethoxy-4-trifluoromethylthiobenzoyl)azetidine-2-carboxylic acid methyl ester
 647857-17-8P, (4-Methoxy-3-trifluoromethylthiophenyl)methanol
 647857-19-0P, Methanesulfonic acid 4-methoxy-3-trifluoromethylthiobenzyl ester 647857-20-3P, (R)-1-(4-Methoxy-3-trifluoromethylthiobenzyl)azetidine-2-carboxylic acid methyl ester 647857-22-5P, (3,4-Dimethoxy-5-trifluoromethylthiophenyl)methanol 647857-23-6P, Methanesulfonic acid
 3,4-dimethoxy-5-trifluoromethylthiobenzyl ester 647857-24-7P, (R)-1-(3,4-Dimethoxy-5-trifluoromethylthiobenzyl)azetidine-2-carboxylic acid methyl ester 647857-26-9P, Methanesulfonic acid
 3-trifluoromethylthiobenzyl ester 647857-27-0P, (R)-1-(3-Trifluoromethylthiobenzyl)azetidine-2-carboxylic acid methyl ester
 647857-29-2P, (R)-1-(3-Trifluoromethylthiobenzoyl)pyrrolidine-2-carboxylic acid methyl ester 647857-31-6P, (R)-1-(3-Methoxy-5-trifluoromethylthiobenzoyl)pyrrolidine-2-carboxylic acid methyl ester
 647857-33-8P, (R)-1-(4-Methoxy-3-trifluoromethylthiobenzoyl)pyrrolidine-2-carboxylic acid methyl ester 647857-35-0P, (R)-1-(3,4-Dimethoxy-5-trifluoromethylthiobenzoyl)pyrrolidine-2-carboxylic acid methyl ester
 647857-37-2P, (R)-1-(4-Methoxy-3-propyl-5-trifluoromethylthiobenzoyl)pyrrolidine-2-carboxylic acid methyl ester 647857-39-4P 647857-40-7P,
 (2R,4S)-1-(3,4-Dimethoxy-5-trifluoromethylthiobenzoyl)-4-fluoropyrrolidine-2-carboxylic acid methyl ester 647857-43-0P 647857-44-1P,
 (2R,4R)-1-(3,4-Dimethoxy-5-trifluoromethylthiobenzoyl)-4-fluoropyrrolidine-2-carboxylic acid methyl ester 647857-45-2P 647857-47-4P
 647857-48-5P, (2R,4R)-1-(3,4-Dimethoxy-5-trifluoromethylthiobenzoyl)-4-methoxypyrrrolidine-2-carboxylic acid methyl ester 647857-50-9P,
 (2R,4S)-4-Benzoyloxy-1-tritylpyrrolidine-2-carboxylic acid methyl ester
 647857-51-0P, (2R,4S)-4-Hydroxy-1-tritylpyrrolidine-2-carboxylic acid methyl ester 647857-52-1P, (2R,4S)-1-(3,4-Dimethoxy-5-trifluoromethylthiobenzoyl)-4-hydroxypyrrrolidine-2-carboxylic acid methyl ester
 647857-54-3P 647857-55-4P 647857-56-5P 647857-57-6P,
 (R)-1-(3,4-Dimethoxy-5-trifluoromethylthiobenzoyl)-4-ethynyl-2,5-dihydro-1H-pyrrole-2-carboxylic acid methyl ester 647857-59-8P,
 (R)-1-(3,4-Dimethoxy-5-trifluoromethylthiobenzoyl)-2,5-dihydro-1H-pyrrole-2-carboxylic acid methyl ester 647857-60-1P 647857-61-2P
 647857-63-4P 647857-64-5P, (2R,4R)-1-(3,4-Dimethoxy-5-trifluoromethylthiobenzoyl)-4-trifluoromethylpyrrolidine-2-carboxylic acid

methyl ester **647857-66-7P 647857-67-8P**,
 (2R,4S)-1-(3,4-Dimethoxy-5-(trifluoromethylthio)benzoyl)-4-[(naphthalen-2-yl)oxy]pyrrolidine-2-carboxylic acid methyl ester **647857-69-0P**
647857-70-3P, (2R,4S)-4-[(Biphenyl-4-yl)oxy]-1-(3,4-dimethoxy-5-trifluoromethylthio)benzoylpyrrolidine-2-carboxylic acid methyl ester
647857-72-5P, (2R,4R)-4-[(Biphenyl-4-yl)oxy]-1-(3,4-dimethoxy-5-trifluoromethylthio)benzoylpyrrolidine-2-carboxylic acid methyl ester
647857-74-7P

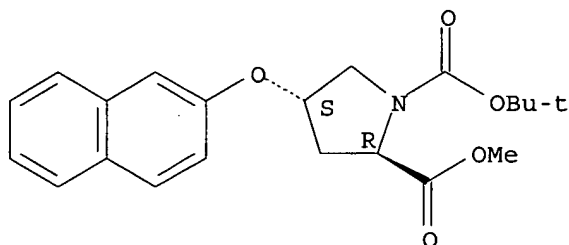
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate; preparation of azetidinecarboxylic acid and pyrrolidinecarboxylic acid N-hydroxyamide derivs. as antibacterial agents)

IT **647857-66-7P 647857-67-8P**, (2R,4S)-1-(3,4-Dimethoxy-5-trifluoromethylthio)benzoyl)-4-[(naphthalen-2-yl)oxy]pyrrolidine-2-carboxylic acid methyl ester
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate; preparation of azetidinecarboxylic acid and pyrrolidinecarboxylic acid N-hydroxyamide derivs. as antibacterial agents)

RN **647857-66-7 CAPLUS**

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-, 1-(1,1-dimethylethyl) 2-methyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

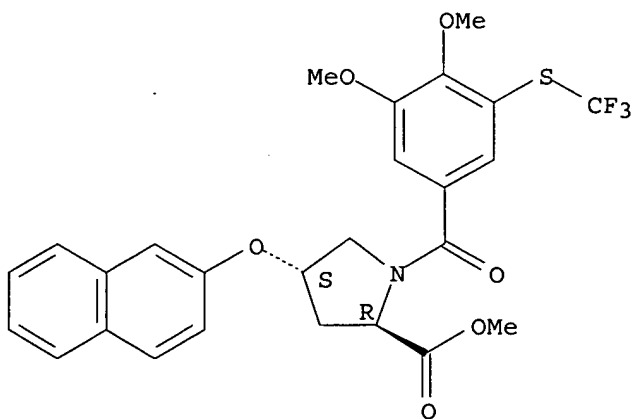
Absolute stereochemistry.



RN **647857-67-8 CAPLUS**

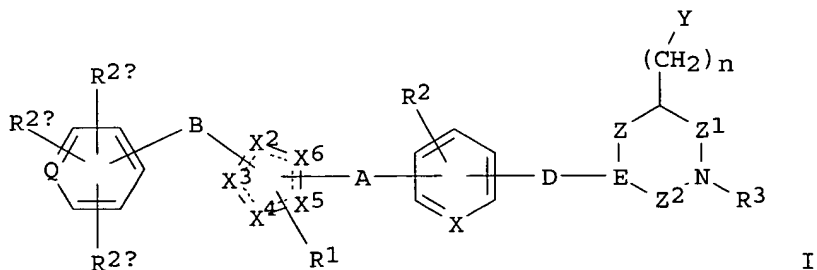
CN D-Proline, 1-[3,4-dimethoxy-5-[(trifluoromethyl)thio]benzoyl]-4-(2-naphthalenyloxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 13 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:41231 CAPLUS
 DOCUMENT NUMBER: 140:111429
 TITLE: Preparation of substituted heterocyclic derivatives
 useful as antidiabetic and antiobesity agents
 INVENTOR(S): Cheng, Peter T. W.; Chen, Sean; Devasthale, Pratik;
 Ding, Charles Z.; Herpin, Timothy F.; Wu, Shung;
 Zhang, Hao; Wang, Wei; Ye, Xiang-Yang
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 543 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004665	A2	20040115	WO 2003-US22149	20030702
WO 2004004665	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG				
JP 2005536494	T2	20051202	JP 2004-520148	20030702
US 2004063700	A1	20040401	US 2003-616365	20030708
NO 2005000077	A	20050203	NO 2005-77	20050106
PRIORITY APPLN. INFO.:			US 2002-394508P	P 20020709
			WO 2003-US22149	W 20030702
OTHER SOURCE(S):			MARPAT 140:111429	
GI				



AB The title compds. (I) [Z1 = (CH2)q, CO; Z2 = (CH2)p, CO; D = CH, CO, (CH2)m (where m = 0-3; p = 1, 2; q = 0-2); n = 0-2; Q = C, N; A = (CH2)x (where x = 1-5); A = (CH2)x1 (where x1 = 1-5) with an alkenyl bond or an alkynyl bond embedded anywhere in the chain; or A = -(CH2)x2-O-(CH2)x3-

hyperinsulinemia,

IC	ICM	A61K
----	-----	------

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s) : 1

Searched by John DiNatale 571-272-2557

647001-90-9P	647001-91-0P	647001-92-1P	647001-93-2P	647001-94-3P
647001-95-4P	647001-96-5P	647001-97-6P	647001-98-7P	647001-99-8P
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647003-58-5P	647003-59-6P	647003-60-9P	647003-61-0P	647003-62-1P
647003-63-2P				

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of substituted heterocyclic derivs. as antidiabetic and
antiobesity agents)

IT	647005-63-8P	647005-64-9P	647005-65-0P	647005-66-1P	647005-67-2P
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647832-90-4P	647832-91-5P			

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 647001-81-8P 647001-82-9P

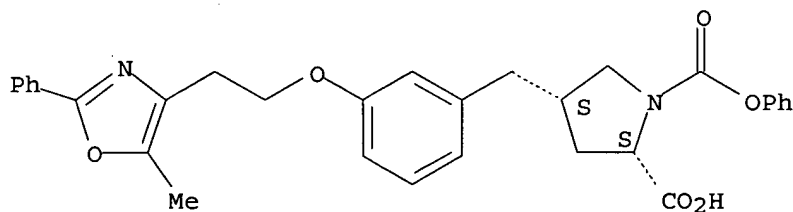
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

RN 647001-81-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[[[3-[2-(5-methyl-2-phenyl-4-oxazolyl)ethoxy]phenyl]methyl]-, 1-phenyl ester, (2R,4R)-rel- (9CI) (CA INDEX NAME)

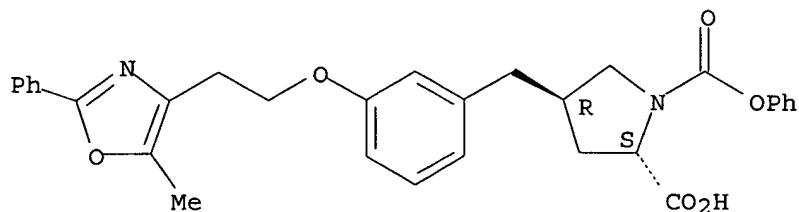
Relative stereochemistry.



RN 647001-82-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[[[3-[2-(5-methyl-2-phenyl-4-oxazolyl)ethoxy]phenyl]methyl]-, 1-phenyl ester, (2R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



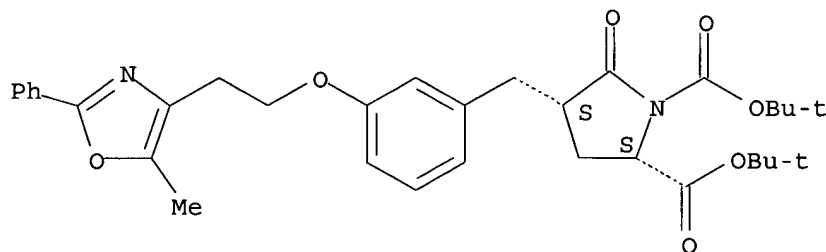
IT 647006-12-0P 647006-13-1P 647006-14-2P
647006-16-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of substituted heterocyclic derivs. as antidiabetic and
antiobesity agents)

RN 647006-12-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[[3-[2-(5-methyl-2-phenyl-4-oxazolyl)ethoxy]phenyl]methyl]-5-oxo-, bis(1,1-dimethylethyl) ester,
(2R,4R)-rel- (9CI) (CA INDEX NAME)

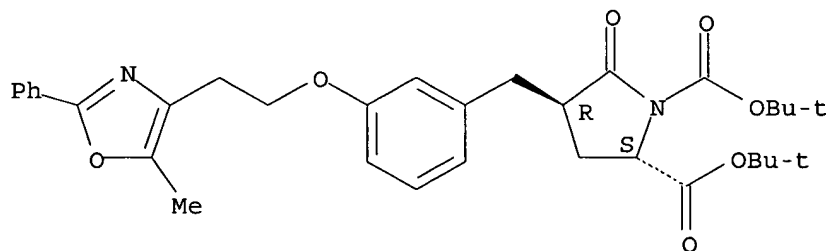
Relative stereochemistry.



RN 647006-13-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[[3-[2-(5-methyl-2-phenyl-4-oxazolyl)ethoxy]phenyl]methyl]-5-oxo-, bis(1,1-dimethylethyl) ester,
(2R,4S)-rel- (9CI) (CA INDEX NAME)

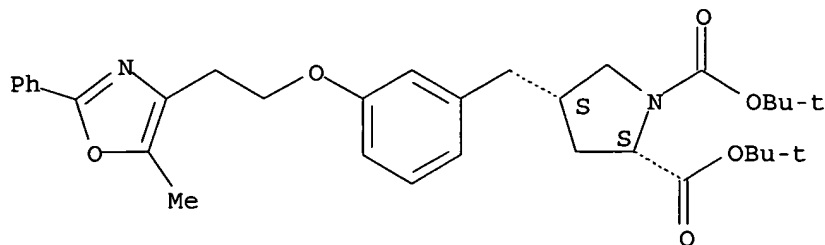
Relative stereochemistry.



RN 647006-14-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[[3-[2-(5-methyl-2-phenyl-4-oxazolyl)ethoxy]phenyl]methyl]-, bis(1,1-dimethylethyl) ester,
(2R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 647006-16-4 CAPLUS

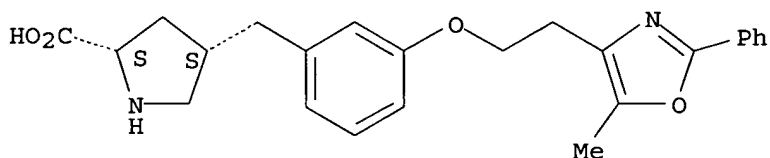
CN D-Proline, 4-[[3-[2-(5-methyl-2-phenyl-4-oxazolyl)ethoxy]phenyl]methyl]-, (4R)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 647006-15-3

CMF C24 H26 N2 O4

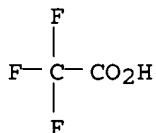
Relative stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



L47 ANSWER 14 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:960534 CAPLUS

DOCUMENT NUMBER: 140:141546

TITLE: NMR Structural Characterization of Peptide Inhibitors Bound to the Hepatitis C Virus NS3 Protease: Design of a New P2 Substituent

AUTHOR(S): Goudreau, Nathalie; Cameron, Dale R.; Bonneau, Pierre; Gorys, Vida; Plouffe, Celine; Poirier, Martin; Lamarre, Daniel; Llinas-Brunet, Montse

CORPORATE SOURCE: Departments of Chemistry and Biological Sciences, Research & Development, Boehringer-Ingelheim (Canada) Ltd., Laval, QC, H7S 2G5, Can.

SOURCE: Journal of Medicinal Chemistry (2004), 47(1), 123-132

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 140:141546

AB A comparative NMR conformational anal. of three distinct tetrapeptide inhibitors of the Hepatitis C NS3 protease that differ at the 4-aryloxy-substituted P2 proline position was undertaken. Specifically, transferred nuclear Overhauser effect expts. in combination with restrained systematic conformational searches were used to characterize the orientation of the P2 aryl substituents of these inhibitors when bound to the NS3 protease. Differences between free and bound conformations were also investigated. Anal. of the results allowed the design of a new P2 aromatic substituent, which significantly increased the potency of our inhibitors. The bound conformation of a specific competitive inhibitor having this novel P2 substituent is also described, along with a model of this inhibitor bound to the NS3 protease. This NS3 protease/inhibitor complex model also supports a hypothetical stabilization role for the P2 residue of the substrates and/or inhibitors and further elucidates the subtle details of the binding of the P2 residue of substrate-based inhibitors.

CC 7-3 (Enzymes)

Section cross-reference(s): 1

IT 72784-43-1 102195-79-9 132622-90-3 159700-58-0 **652160-93-5**
 652160-94-6 652160-95-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(design of improved P2 substituent in peptide inhibitor of Hepatitis C virus NS3 protease)

IT **254883-52-8P** 259214-64-7P 652160-92-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(design of improved P2 substituent in peptide inhibitor of Hepatitis C virus NS3 protease)

IT **652160-93-5**

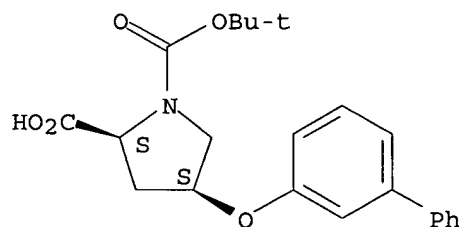
RL: RCT (Reactant); RACT (Reactant or reagent)

(design of improved P2 substituent in peptide inhibitor of Hepatitis C virus NS3 protease)

RN 652160-93-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-([1,1'-biphenyl]-3-yloxy)-, 1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **254883-52-8P**

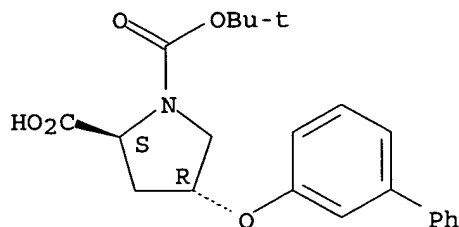
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(design of improved P2 substituent in peptide inhibitor of Hepatitis C virus NS3 protease)

RN 254883-52-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-([1,1'-biphenyl]-3-yloxy)-, 1-(1,1-dimethylethyl) ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 15 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:950834 CAPLUS

DOCUMENT NUMBER: 140:16975

TITLE: Preparation of peptides as hepatitis C virus inhibitors

INVENTOR(S): Wang, Xiangdong Alan; Sun, Li-Quang; Sit, Sing-Yuen; Sin, Ny; Scola, Paul Michael; Hewawasam, Piyasena; Good, Andrew Charles; Chen, Yan; Campbell, Jeffrey Allen

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 675 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099274	A1	20031204	WO 2003-US15755	20030520
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2486308	AA	20031204	CA 2003-2486308	20030520
AU 2003241510	A1	20031212	AU 2003-241510	20030520
US 2004106559	A1	20040603	US 2003-441657	20030520
US 6995174	B2	20060207		
EP 1505963	A1	20050216	EP 2003-731248	20030520
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
BR 2003011132	A	20050308	BR 2003-11132	20030520
JP 2005533028	T2	20051104	JP 2004-506798	20030520
NO 2004004807	A	20041216	NO 2004-4807	20041104
PRIORITY APPLN. INFO.:			US 2002-382055P	20020520
			WO 2003-US15755	20030520

OTHER SOURCE(S): MARPAT 140:16975

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Peptides I [R1 = alkyl, cycloalkyl, alkylcycloalkyl; m, n = 1 or 2; R2 = H, (halo)alk(en)yl, (halo)cycloalkyl; R3 = (un)substituted alkyl or together with the carbon atom to which it is attached forms cycloalkyl optionally substituted by alkenyl; R4 = (un)substituted (hetero)aryl; X = O, S, SO, SO₂, OCH₂, CH₂O, NH; Y = H, (nitro)pyridyl, (nitro)phenyl, alkyl optionally substituted with cyano, OH, or cycloalkyl; B = H, alkyl, acyl, (thio)carbamoyl, sulfonyl, or sulfamoyl groups (with provisos)] or their pharmaceutically-acceptable salts or prodrugs were prepared for the treatment of hepatitis C virus (HCV) infection. Thus, compound II (Boc = tert-butoxycarbonyl) was prepared by a multistep procedure and assayed for inhibition of HCV NS3/4A protease (IC₅₀ and EC₅₀ < 0.1 μM).

IC ICM A61K031-40

ICS C07D207-27; C07D207-452; C07D295-00

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 63

IT	630424-80-5	630424-81-6	630424-82-7	630424-83-8	630424-84-9
	630424-85-0	630424-86-1	630424-87-2	630424-88-3	630424-89-4
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	630425-45-5	630425-46-6	630425-47-7	630425-48-8	
	630425-49-9	630425-50-2	630425-51-3	630425-52-4	

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of peptides as hepatitis C virus inhibitors)

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	630422-89-8P	630422-90-1P	630422-91-2P	630422-92-3P	630422-93-4P
	630422-94-5P	630422-95-6P	630422-96-7P	630422-97-8P	630422-98-9P
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	630423-03-9P	630423-04-0P	630423-05-1P	630423-06-2P	630423-07-3P
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630425-60-4P	630426-50-5P	630426-51-6P	630426-52-7P	630426-53-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of peptides as hepatitis C virus inhibitors)

IT 630425-44-4 630425-45-5

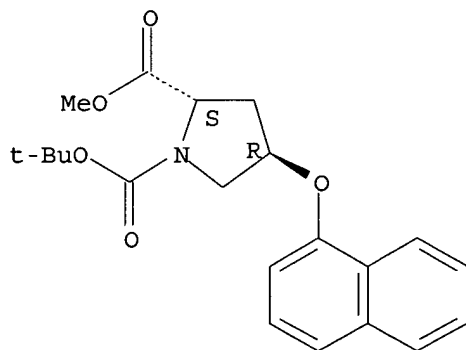
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of peptides as hepatitis C virus inhibitors)

RN 630425-44-4 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(1-naphthalenyloxy)-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

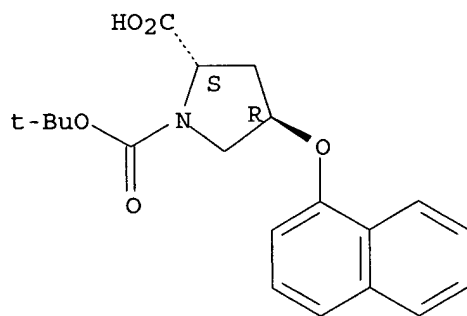
Absolute stereochemistry.



RN 630425-45-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(1-naphthalenyloxy)-, 1-(1,1-dimethylethyl) ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 630423-01-7P 630423-98-2P 630423-99-3P
630424-00-9P

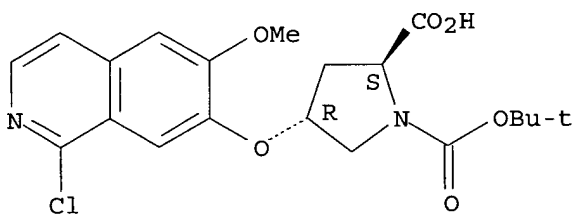
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of peptides as hepatitis C virus inhibitors)

RN 630423-01-7 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(1-chloro-6-methoxy-7-
isoquinolinyloxy]-, 1-(1,1-dimethylethyl) ester, (2S,4R)- (9CI) (CA
INDEX NAME)

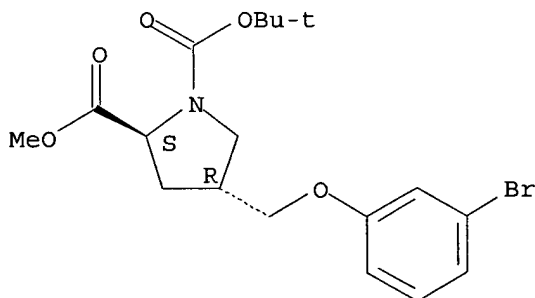
Absolute stereochemistry.



RN 630423-98-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-bromophenoxy)methyl]-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

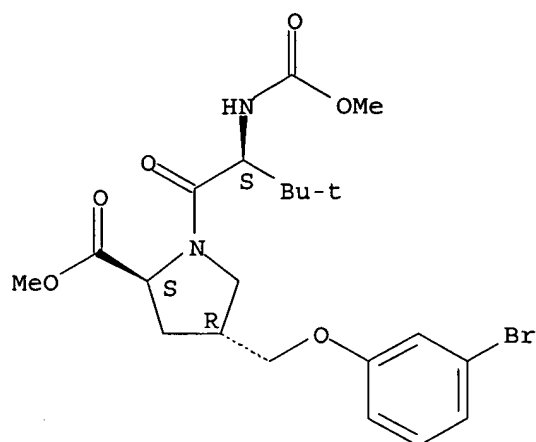
Absolute stereochemistry.



RN 630423-99-3 CAPLUS

CN L-Proline, N-(methoxycarbonyl)-3-methyl-L-valyl-4-[(3-bromophenoxy)methyl]-,
methyl ester, (4R)- (9CI) (CA INDEX NAME)

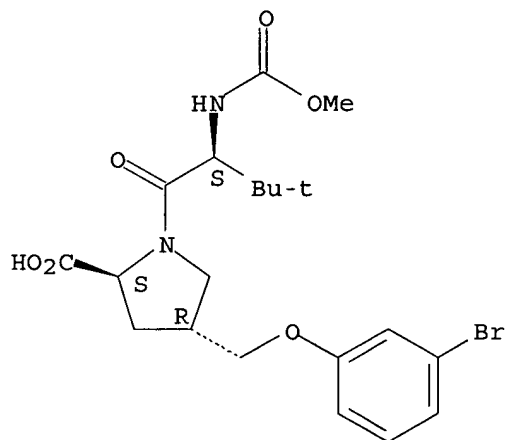
Absolute stereochemistry.



RN 630424-00-9 CAPLUS

CN L-Proline, N-(methoxycarbonyl)-3-methyl-L-valyl-4-[(3-bromophenoxy)methyl]-, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 16 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:796670 CAPLUS

DOCUMENT NUMBER: 139:307787

TITLE: Preparation of 4-anilinoquinazolines as antiproliferative agents

INVENTOR(S): Bradbury, Robert Hugh; Hennequin, Laurent Francois Andre; Kettle, Jason Grant

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 190 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

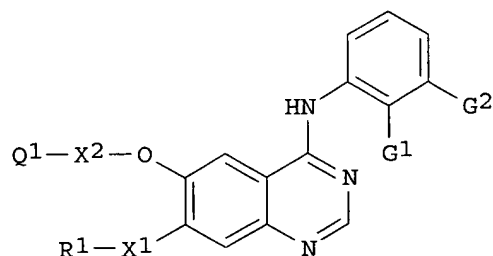
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082831	A1	20031009	WO 2003-GB1306	20030326
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2479642	AA	20031009	CA 2003-2479642	20030326
AU 2003214443	A1	20031013	AU 2003-214443	20030326
EP 1487806	A1	20041222	EP 2003-710015	20030326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008670	A	20050201	BR 2003-8670	20030326
JP 2005529092	T2	20050929	JP 2003-580299	20030326
US 2005215574	A1	20050929	US 2004-508675	20040922
NO 2004004325	A	20041216	NO 2004-4325	20041012
PRIORITY APPLN. INFO.:				
			GB 2002-7323	A 20020328
			GB 2002-30086	A 20021224
			GB 2003-1916	A 20030128
			WO 2003-GB1306	W 20030326

OTHER SOURCE(S): MARPAT 139:307787
GI



AB The title compds. [I; G1, G2 = halo; X1 = a bond, O; R1 = H, alkyl, haloalkyl, etc.; X2 = a bond, (CR₂R₃)_m (m = 1-6; R₂, R₃ = H, OH, alkyl, hydroxyalkyl); Q1 = (un)substituted cycloalkyl, heterocyclyl] and their pharmaceutically acceptable salts, useful as an antiproliferative agent in the prevention or treatment of tumors which are sensitive to inhibition of erbB receptor tyrosine kinases, were prepared and formulated. Thus, reacting 4-(3-chloro-2-fluorophenyl)-6-hydroxy-7-methoxyquinazoline (preparation given) with 1-methyl-3-pyrrolidinol in the presence of PPh₃ and di-tert-Bu azodicarboxylate in DCM afforded 16% I.HCl [G1 = F; G2 = Cl; X1 = O; R1 = Me; X2 = a bond; Q1 = 1-methylpyrrolidin-3-yl]. The compds. I showed IC₅₀ in the range of 0.001-10 μM in EGFR tyrosine kinase phosphorylation assay.

IC ICM C07D239-94
ICS C07D401-12; C07D401-14; C07D403-14; C07D491-04; A61K031-517; A61P035-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 73286-70-1P 86953-79-9P 298681-10-4P 352278-31-0P 574745-97-4P
 612501-45-8P 612501-46-9P 612501-47-0P 612501-48-1P 612501-49-2P
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 612501-70-9P **612501-71-0P 612501-72-1P**
612501-73-2P 612501-74-3P 612501-75-4P 612501-76-5P
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 612501-82-3P 612501-83-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 4-anilinoquinazolines as antiproliferative agents)

IT **612501-71-0P 612501-72-1P 612501-73-2P**
612501-74-3P

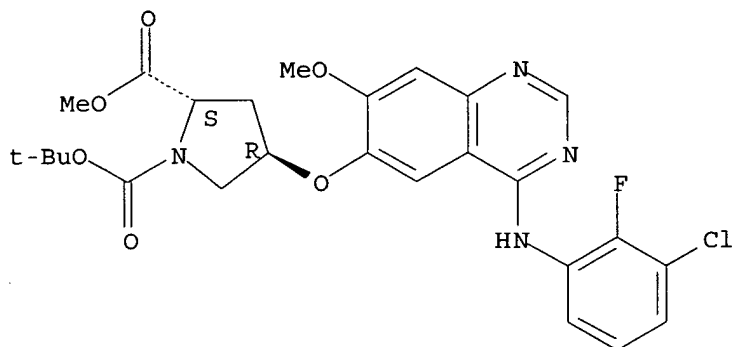
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 4-anilinoquinazolines as antiproliferative agents)

RN 612501-71-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

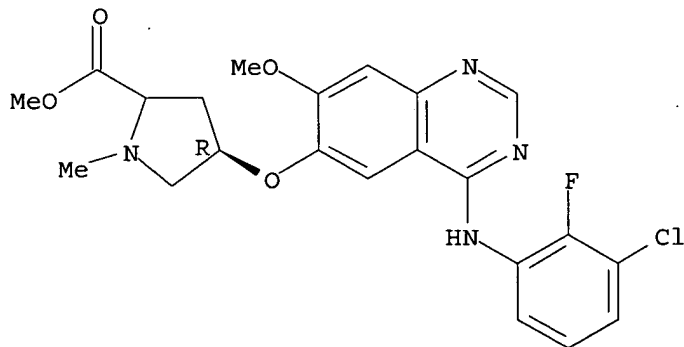
Absolute stereochemistry.



RN 612501-72-1 CAPLUS

CN Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

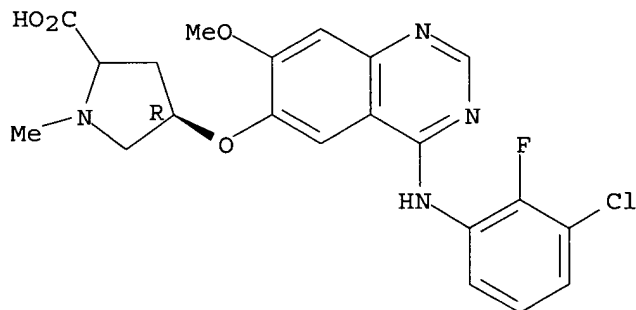
Absolute stereochemistry.



RN 612501-73-2 CAPLUS

CN Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, (4R)- (9CI) (CA INDEX NAME)

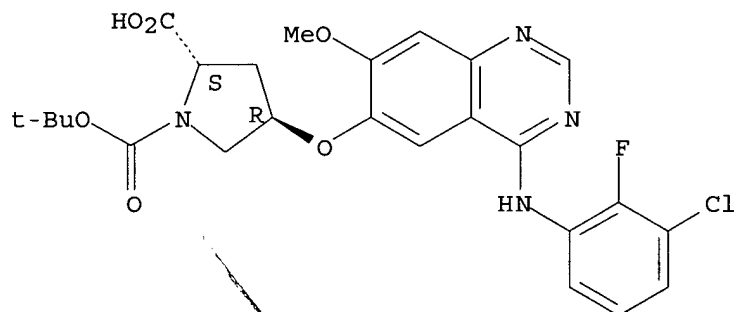
Absolute stereochemistry.



RN 612501-74-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-, 1-(1,1-dimethylethyl) ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 17 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:663930 CAPLUS

DOCUMENT NUMBER: 139:307981

TITLE: Synthesis of Functionally Diverse and Conformationally Constrained Polycyclic Analogues of Proline and Prolinol

AUTHOR(S): Hanessian, Stephen; Papeo, Gianluca; Angiolini, Mauro; Fattis, Kamal; Beretta, Marco; Munro, Alexander

CORPORATE SOURCE: Department of Chemistry, Université de Montreal, Montreal, QC, H3G 3J7, Can.

SOURCE: Journal of Organic Chemistry (2003), 68(19), 7204-7218 CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:307981

AB Alkylation of the monoenolate of N-Boc-L-pyrogutamic acid Me ester with a

variety of benzylic halides and their homologs gave the corresponding anti-C-4-alkylated products as major products. Formation of the N-Boc-iminium ion and Friedel-Crafts intramol. cationic ring closure afforded a series of fused 1-azacyclodihydroindene derivs. with interesting topologies. Functional diversity was introduced via further manipulation of pendant groups on the original proline motif as well as on the aromatic moiety.

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 27, 75

IT 27561-51-9P 149104-89-2P 612066-86-1P **612066-87-2P**
 612066-88-3P 612066-90-7P 612066-91-8P 612066-93-0P 612066-96-3P
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 612067-51-3P 612067-52-4P 612067-53-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of conformationally constrained polycyclic analogs of proline and prolinol starting from alkylation of pyroglutamate)

IT **612066-87-2P 612067-14-8P 612067-34-2P**
612067-43-3P

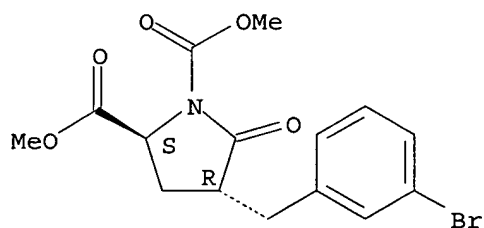
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of conformationally constrained polycyclic analogs of proline and prolinol starting from alkylation of pyroglutamate)

RN 612066-87-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-bromophenyl)methyl]-5-oxo-, dimethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

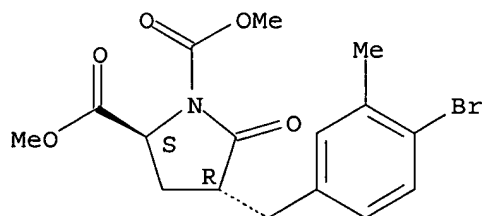
Absolute stereochemistry. Rotation (-).



RN 612067-14-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(4-bromo-3-methylphenyl)methyl]-5-oxo-, dimethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

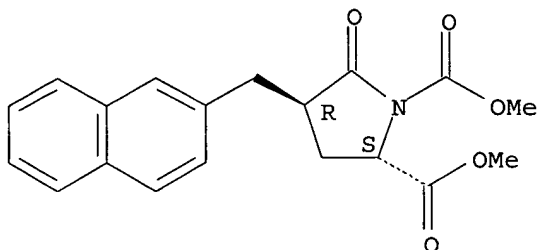
Absolute stereochemistry. Rotation (-).



RN 612067-34-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenylmethyl)-5-oxo-, dimethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

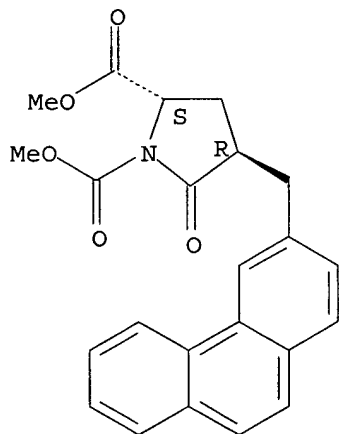
Absolute stereochemistry.



RN 612067-43-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 5-oxo-4-(3-phenanthrenylmethyl)-, dimethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 18 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:645219 CAPLUS

DOCUMENT NUMBER: 140:224

TITLE: How a single inversion of configuration leads to a reversal of the binding mode: proposal of a novel arrangement of CCK2 ligands in their receptor, and contribution to the development of peptidomimetic or non-peptide CCK2 ligands

AUTHOR(S): Bellier, Bruno; Garbay, Christiane

CORPORATE SOURCE: Faculte de Pharmacie, Laboratoire de Pharmacochimie Moleculaire et Structurale, CNRS FRE 2463, INSERM U266, Paris, 75270, Fr.

SOURCE: European Journal of Medicinal Chemistry (2003), 38(7-8), 671-686
CODEN: EJMCA5; ISSN: 0223-5234

PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 140:224

AB The implication of CCK2 receptors in crucial physiol. functions has driven the search for synthetic ligands of this receptor. A notable rationale starting from CCK-4 (minimal endogenous CCK2 agonist), the dipeptoid strategy, led to potent CCK2 antagonists exemplified by CI-988. However, careful examination of the literature enlightened several incompatibilities between the proposed recognition mode of the receptor by such compds. (or peptide analogs) and exptl. data. Thus, we hypothesized that CCK2 dipeptoid' antagonists bind the receptor in a mode opposite to that previously suggested. The reexamn. of numerous published data, supported by the characterization of new hybrid' compds., brought out strong evidence that this reverse' mode truly characterizes CCK2 dipeptoid' antagonists. These findings renew the perspectives of further chemical development of CCK2 ligands, e.g. non-peptidic agonists.

CC 1-3 (Pharmacology)

Section cross-reference(s): 2

IT **701976-04-7** 35856-00-9P 36635-61-7P 42067-67-4P,
 Tricyclo[3.3.1.1^{3,7}]decane-2-methanamine **198969-06-1P** -
 627872-12-2P 627872-17-7P 627872-18-8P 627872-19-9P 627872-23-5P
 627872-24-6P 627872-34-8P

RL: RCT (Reactant); SPN (Synthetic preparation)

(single configurational inversion leads to a reversal of the binding mode of CCK2 ligands to receptors and development of peptidomimetic or non-peptide CCK2 ligands)

IT **701976-06-9** 627872-13-3P 627872-14-4P 627872-15-5P
 627872-16-6P 627872-20-2P 627872-21-3P 627872-25-7P 627872-26-8P
 627872-27-9P 627872-35-9P 627872-36-0P 627872-37-1P
701976-05-8P

RL: SPN (Synthetic preparation)

(single configurational inversion leads to a reversal of the binding mode of CCK2 ligands to receptors and development of peptidomimetic or non-peptide CCK2 ligands)

IT **701976-04-7 198969-06-1P**

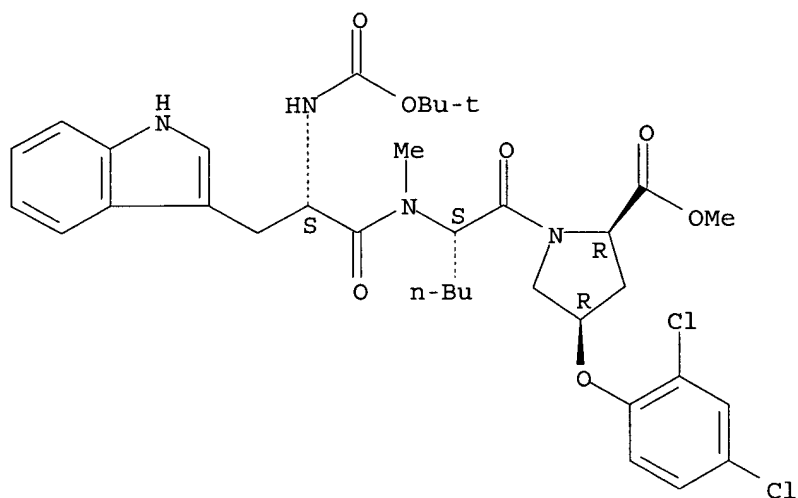
RL: RCT (Reactant); SPN (Synthetic preparation)

(single configurational inversion leads to a reversal of the binding mode of CCK2 ligands to receptors and development of peptidomimetic or non-peptide CCK2 ligands)

RN 701976-04-7 CAPLUS

CN D-Proline, N-[(1,1-dimethylethoxy)carbonyl]-L-tryptophyl-N-methyl-L-norleucyl-4-(2,4-dichlorophenoxy)-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 198969-06-1 CAPLUS

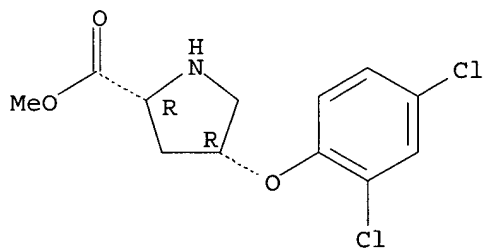
CN D-Proline, 4-(2,4-dichlorophenoxy)-, methyl ester, (4R)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 198969-05-0

CMF C12 H13 Cl2 N O3

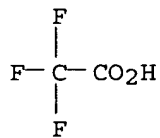
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 701976-06-9 701976-05-8P

RL: SPN (Synthetic preparation)

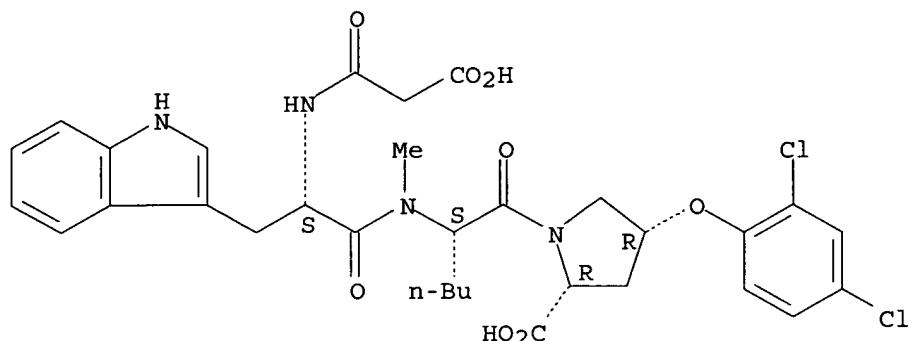
(single configurational inversion leads to a reversal of the binding

mode of CCK2 ligands to receptors and development of peptidomimetic or non-peptide CCK2 ligands)

RN 701976-06-9 CAPLUS

CN D-Proline, N-(carboxyacetyl)-L-tryptophyl-N-methyl-L-norleucyl-4-(2,4-dichlorophenoxy)-, (4R)-(9CI) (CA INDEX NAME)

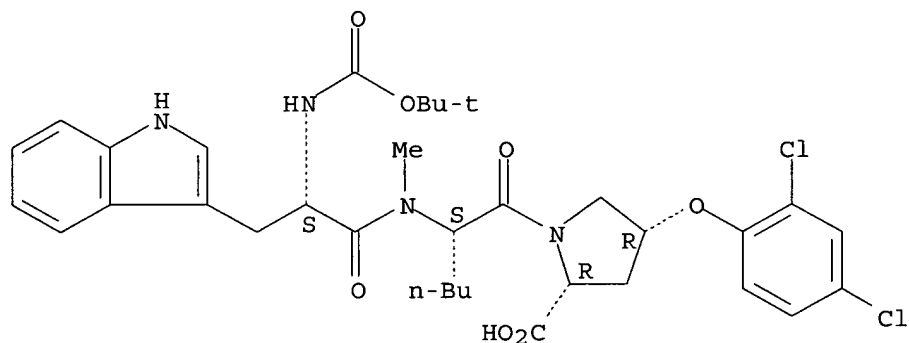
Absolute stereochemistry.



RN 701976-05-8 CAPLUS

CN D-Proline, N-[(1,1-dimethylethoxy)carbonyl]-L-tryptophyl-N-methyl-L-norleucyl-4-(2,4-dichlorophenoxy)-, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 19 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:435318 CAPLUS

DOCUMENT NUMBER: 139:22213

TITLE: Preparation of substituted cyclic amines as metalloprotease inhibitors

INVENTOR(S): Natchus, Michael George; De, Biswanath; Pikul, Stanislaw; Almstead, Neil Gregory; Bookland, Roger Gunnard; Taiwo, Yetunde Olabisi; Cheng, Menyan

PATENT ASSIGNEE(S): The Procter & Gamble Company, USA

SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 888,675.

CODEN: USXXCO

DOCUMENT TYPE: Patent

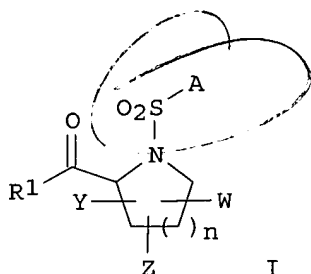
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003105153	A1	20030605	US 2002-186531	20020701
US 6872742	B2	20050329		
US 6417219	B1	20020709	US 1997-918317	19970826
US 2002061877	A1	20020523	US 2001-888675	20010625
US 6569855	B2	20030527		
US 2002072517	A1	20020613	US 2001-888759	20010625
US 2003191163	A1	20031009	US 2002-308780	20021203
US 6858628	B2	20050222		
JP 2004115531	A2	20040415	JP 2003-384116	20031113
US 2004138260	A1	20040715	US 2003-730572	20031208
US 2005101567	A1	20050512	US 2004-3594	20041203
US 2005154019	A1	20050714	US 2004-3884	20041203
US 2005137248	A1	20050623	US 2005-59107	20050216
PRIORITY APPLN. INFO.:			US 1996-24842P	P 19960828
			US 1997-918317	A2 19970826
			US 2001-888675	A2 20010625
			US 2001-888759	A2 20010625
			JP 1998-511715	A3 19970822
			US 2002-186531	A2 20020701
			US 2002-308780	A3 20021203

OTHER SOURCE(S) : MARPAT 139:22213
GI



AB The invention provides compds. having a structure according to formula (I) [wherein A = each (un)substituted alkyl, heteroalkyl, aryl, heteroaryl; R1 = NHOR2 (where R2 = hydrogen or alkyl); W = H, lower alkyl, or an alkylene bridge that forms a ring in addition to the ring depicted in the formula; Y = HO, SR3, SOR4, SO2R8, alkoxy, (un)substituted NH2; R4 = alkyl, aryl, heteroaryl; R8 = alkyl, aryl, heteroaryl, heteroalkyl, amino, alkylamino, dialkylamino, arylamino, diarylamino, alkylaryl amino; Z = H, HO, alkyl, or an alkylene or heteroalkylene bridge that forms a ring in addition to the ring depicted in the formula; n = 1; provisos given] or pharmaceutically acceptable salts, or biohydrolyzable amides, esters, or imides thereof. These compds. are useful as inhibitors of metalloproteases, in particular zinc metalloprotease, and effective in treating conditions characterized by excess activity of these enzymes, e.g. degenerative diseases such as arthritis and multiple sclerosis and inflammation (no data). Thus, cis-Hydroxy-D-proline (50 g, 0.38 mol) was dissolved in water:dioxane (1:1, 300 mL) with Et3N (135 mL, 0.96 mol), treated with 4-Methoxyphenylsulfonyl chloride (87 g, 0.42 mol) along with 2,6-dimethylaminopyridine (4.6 g, 0.038 mol), stirred for 14 h at room temperature, concentrated, and diluted with EtOAc to give, after workup,

N-(4-Methoxyphenylsulfonyl)-(4R)-hydroxypyrrolidine-(2R)-carboxylic acid. This intermediate was dissolved in MeOH (500 mL), treated dropwise with 50 mL SOCl₂, stirred for 14 h, evaporated, to dryness, and triturated with CHCl₃ to give N-4-Methoxyphenylsulfonyl-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine as a white solid which was sufficiently pure to carry forward without purification. The latter Me ester (361 mg, 1.15 mmol) was taken in 1 mL MeOH, treated with NH₂OK (1.45 mL, 0.86 M in methanol), and stirred overnight to give, after workup, N-4-Methoxyphenylsulfonyl-(2R)-N-hydroxycarboxamido-(4S)-hydroxypyrrolidine.

IC ICM A61K031-4025
ICS A61K031-401

INCL 514422000; 514423000

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 7, 27

IT 1138-54-1P, 4-(Isobutoxy)phenylsulfonyl chloride 57850-07-4P,
N-(4-Methylphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine
203934-42-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-4-
oxopyrrolidine 203934-63-8P 203934-71-8P 203994-66-5P,
N-(4-Methoxyphenylsulfonyl)-(2R)-carboxy-(4R)-hydroxypyrrolidine
203994-80-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
hydroxypyrrolidine 203994-82-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4S)-acetylthiopyrrolidine 204072-15-1P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-
benzoyloxypyrrolidine 204072-16-2P, N-(4-Methoxyphenylsulfonyl)-(2S)-
methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-17-3P,
N-(4-Methoxyphenylsulfonyl)-(2S)-methoxycarbonyl-(4S)-hydroxypyrrolidine
204072-18-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-carboxy-(4S)-
hydroxypyrrolidine 204072-19-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4S)-methoxypyrrolidine 204072-20-8P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
(trifluoromethanesulfonyloxy)pyrrolidine 204072-21-9P 204072-23-1P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-[(benzothiazol-2-
yl)thio]pyrrolidine 204072-24-2P, N-(4-Methoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4S)-[N-methyl-2-imidazolylthio]pyrrolidine
204072-25-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-[N-
methyl-2-imidazolylthio]pyrrolidine 204072-26-4P, N-(4-
Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-phenoxy-pyrrolidine
204072-27-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(4-
benzyloxyphenoxy)pyrrolidine 204072-28-6P, N-(4-
Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-
phenylaminophenoxy)pyrrolidine 204072-29-7P, N-(4-Methoxyphenylsulfonyl)-
(2R)-methoxycarbonyl-(4S)-(3-pyridinyloxy)pyrrolidine 204072-30-0P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-
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N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(4-
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(2R)-methoxycarbonyl-(4S)-(3-methoxyphenylthio)pyrrolidine 204072-36-6P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
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methoxycarbonyl-(4R)-benzyloxymethoxypyrrolidine 204072-38-8P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-[(2-
methoxyethoxy)methoxy]pyrrolidine 204072-39-9P 204072-40-2P,
N-(4-Methoxyphenylsulfonyl)-(2R)-carboxy-4-oxopyrrolidine 204072-41-3P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-4-hydroxy-4-
ethylpyrrolidine 204072-42-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4R)-4-hydroxy-4-phenylpyrrolidine 204072-44-6P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-3,3-dimethyl-4-
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N-(3,4-Dimethoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-47-9P, N-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-49-1P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-benzoyloxypyrrolidine 204072-50-4P, N-(4-Bromobenzenesulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-51-5P, N-(2-Methyl-4-bromobenzenesulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-52-6P, N-(2,4-Dichlorophenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-53-7P, 4-(2-Methoxyethoxy)phenylsulfonyl chloride 204072-55-9P, N-(4-Phenoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-56-0P, N-(4-Isobutyloxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-57-1P, N-(2-Methyl-4-bromophenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-methoxyphenylthio)pyrrolidine 204072-58-2P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2-benzothiazolylthio)pyrrolidine 204072-59-3P, N-(2-Nitro-4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2-benzothiazolylthio)pyrrolidine 204072-60-6P, N-(4-Butoxyphenylsulfonyl)-(2R)-Methoxycarbonyl-(4S)-(4-methoxyphenylthio)pyrrolidine 204072-61-7P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-pyridyloxy)pyrrolidine 204072-62-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-azidopyrrolidine 204072-64-0P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-(methylsulfonyl)pyrrolidine 204072-65-1P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-azidopyrrolidine 204072-66-2P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-aminopyrrolidine 204072-67-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-propylaminopyrrolidine 204072-68-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-n-hexylaminopyrrolidine 204072-69-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2-phenylethylamino)pyrrolidine 204072-70-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(N-butyl-N-hexylamino)pyrrolidine 204072-71-9P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(methanesulfonyl)amino]pyrrolidine 204072-74-2P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(3-pyridylmethyl)amino]pyrrolidine 204072-75-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-(3-pyridylmethyl)-N-(methanesulfonyl)amino]pyrrolidine 204072-76-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N,N-bis(methanesulfonyl)amino]pyrrolidine 204072-77-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-(methanesulfonyl)propylamino]pyrrolidine 204072-78-6P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(4-methoxyphenylsulfonyl)amino]pyrrolidine 204072-79-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-oxohexyl)aminopyrrolidine 204072-81-1P 204072-82-2P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(2R)-1-oxo-2-benzyloxypropyl]amino]pyrrolidine 204072-83-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(2R)-1-oxo-2-benzyloxy-3-phenylpropyl]amino]pyrrolidine 204072-84-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-[(2R)-1-oxo-2-benzyloxypropyl]propylamino]pyrrolidine 204072-85-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-[(2R)-1-oxo-2-hydroxypropyl]propylamino]pyrrolidine 204072-86-6P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-[(2R)-1-oxo-2-benzyloxy-3-phenylpropyl]propylamino]pyrrolidine 204072-87-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-[(2R)-1-oxo-2-hydroxy-3-phenylpropyl]propylamino]pyrrolidine 204072-88-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-piperidyl)pyrrolidine 204072-89-9P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-piperidyl)pyrrolidine 204072-90-2P,

N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-morpholinopyrrolidine 204072-91-3P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-morpholinopyrrolidine 204072-92-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204072-93-5P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204073-01-8P 204073-02-9P 537704-28-2P 537704-31-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-aminopyrrolidine formate 537704-32-8P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[[[N-methyl-3-imidazolyl)sulfonyl]amino]pyrrolidine 537704-35-1P 537704-63-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2,5-dioxo-1-methylimidazolidin-3-yl)pyrrolidine 537704-66-8P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2,5-dioxo-1-methylimidazolidin-3-yl)pyrrolidine 537704-68-0P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-allyl-2,5-dioxoimidazolidin-3-yl)pyrrolidine 537704-72-6P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2,4-dioxo-5,5-dimethylimidazolidin-1-yl)pyrrolidine 537704-74-8P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(5S)-5-methyl-2,4-dioxoimidazolidin-1-yl]pyrrolidine 537704-76-0P, N-[4-(2-Methoxyethoxy)phenylsulfonyl]-(2R)-methoxycarbonyl-(4S)-(3-methyl-2,4-dioxoimidazolidin-1-yl)pyrrolidine 537704-78-2P, N-(4-Phenoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-methyl-2,4-dioxoimidazolidin-1-yl)pyrrolidine

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of substituted cyclic amines as metalloprotease inhibitors for treating conditions characterized by excess activity of these enzymes)

IT 204072-28-6P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-phenylaminophenoxy)pyrrolidine

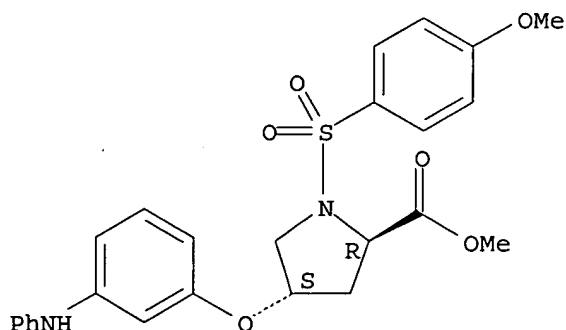
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of substituted cyclic amines as metalloprotease inhibitors for treating conditions characterized by excess activity of these enzymes)

RN 204072-28-6 CAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[3-(phenylamino)phenoxy]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

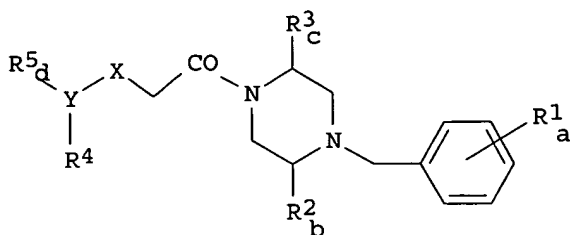


REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

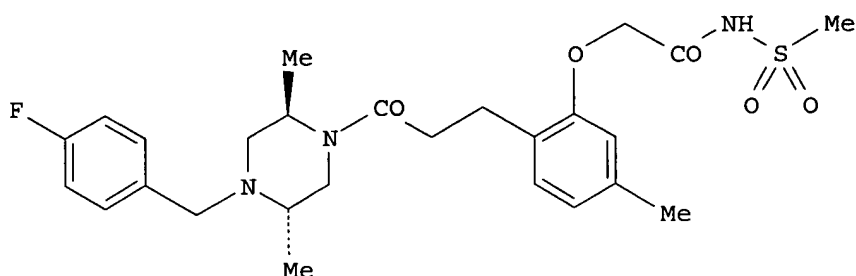
L47 ANSWER 20 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:335088 CAPLUS
 DOCUMENT NUMBER: 138:354006
 TITLE: Preparation of piperazine derivatives with CCR1
 receptor antagonist activity
 INVENTOR(S): Blumberg, Laura Cook; Brown, Matthew Frank; Hayward,
 Matthew Merrill; Poss, Christopher Stanley; Lundquist,
 Gregory Dean, Jr.; Shavnya, Andrei
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA
 SOURCE: PCT Int. Appl., 139 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035627	A1	20030501	WO 2002-IB3989	20020926
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2463272	AA	20030501	CA 2002-2463272	20020926
EP 1438298	A1	20040721	EP 2002-772651	20020926
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EE 200400088	A	20041015	EE 2004-88	20020926
BR 2002013452	A	20041109	BR 2002-13452	20020926
JP 2005507923	T2	20050324	JP 2003-538143	20020926
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ZA 2004002090	A	20050523	ZA 2004-2090	20040316
BG 108674	A	20050430	BG 2004-108674	20040408
NO 2004001631	A	20040526	NO 2004-1631	20040421
PRIORITY APPLN. INFO.:			US 2001-338601P	P 20011022
			WO 2002-IB3989	W 20020926
OTHER SOURCE(S):	MARPAT	138:354006		
GI				



I



II

- AB The present invention relates to piperazine derivs. (shown as I; variables defined below; e.g. N-[[2-[3-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methylphenoxy]acetyl]methanesulfonamide (shown as II)) and the pharmaceutically acceptable forms thereof. Moreover, the present invention is also directed at pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier. Furthermore, the present invention is directed at methods of using the herein described compds. and compns. for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the 15 CCR1 receptor in a mammal. For I: a = 0-5; b = 0-2; c = 0-2; d = 0-4; X = O, S, CH₂, or NR₆; Y = (C₆-C₁₀)aryl or (C₂-C₉)heteroaryl; each R₁ = H, HO, halo, (C₁-C₈)alkyl, (C₁-C₈)alkylo, HO(C₁-C₈)alkyl, NC, H₂N, H₂N(C₁-C₈)alkyl, HO₂C, (C₁-C₈)alkylC(O), (C₁-C₈)alkylC(O)(C₁-C₈)alkyl, H₂NC(O), or H₂NC(O)(C₁-C₈)alkyl. Each R₂ and R₃ = H, oxo, (C₁-C₈)alkyl, (C₃-C₈)cycloalkyl(C₁-C₈)alkyl, (C₆-C₁₀)aryl, etc. R₄ = (HO₂C)(H₂N)(C₁-C₈)alkyl, (HO₂C)[[(C₁-C₈)alkyl]NH](C₁-C₈)alkyl, (HO₂C)[[(C₁-C₈)alkyl]2N](C₁-C₈)alkyl, etc.; R₅ = H, HO, halo, NC, HO₂C, H₂N, (C₁-C₈)alkylNH, [(C₁-C₈)alkyl]2N, etc.; R₆ = H, (C₁-C₈)alkyl, (C₁-C₈)alkylC(O), (C₆-C₁₀)arylC(O), (C₂-C₉)heteroarylC(O), H₂NC(O), (C₁-C₈)alkylNHC(O), [(C₁-C₈)alkyl]2NC(O), (C₁-C₈)alkyloC(O), or (C₁-C₈)alkylSO₂; addnl. details are given in the claims. Although the methods of preparation are not claimed, 47 example preps. and characterization data (mass spectral parent ion mass) for 259 examples of I are included. I are potent and selective inhibitors of MIP-1 α (CCL3) binding to its receptor CCR1 found on inflammatory and immunomodulatory cells (preferably leukocytes and lymphocytes). These compds. also inhibit MIP-1 α (and the related chemokines shown to interact with CCR1)-induced chemotaxis of THP-1 cells and human leukocytes. All I in the examples had IC₅₀ of <10 μ M in the MIP-1 α -induced chemotaxis assay.
- IC ICM C07D241-04
ICS A61K031-495; C07D401-12; A61P029-00
- CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
- IT 519171-77-8P 519171-81-4P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide hydrochloride 519171-85-8P, (2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-

(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid
519171-89-2P, 3-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid
hydrochloride 519171-92-7P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]sulfamoyl]acetic acid
519171-93-8P, 3-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]amino]propionic acid
hydrochloride 519171-96-1P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]-3-(2-methylbenzenesulfonyl)urea 519171-98-3P, (2-Methylbenzenesulfonyl)carbamic acid 5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl ester
519171-99-4P, 2-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]sulfamoyl]propionic acid
519172-00-0P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]oxy]acetyl]methanesulfonamide
519172-04-4P, 1-Acetyl-3-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]sulfamide 519172-06-6P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylidene]amino]oxy]acetic acid 519172-07-7P,
N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519172-09-9P,
N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]sulfamide 519172-10-2P, N-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide 519172-14-6P,
3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid 519172-16-8P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonyl]amino]acetic acid hydrochloride 519172-20-4P,
5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-[(2-propylamino)carbonyl]benzenesulfonamide 519172-21-5P,
5-Chloro-N-(2,2-dimethylpropionyl)-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonamide 519172-22-6P,
5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-(2-hydroxy-2-methylpropionyl)benzenesulfonamide
519172-24-8P, N-Acetyl-C-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide
519172-30-6P, C-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(2-hydroxy-2-methylpropionyl)methanesulfonamide 519172-32-8P, C-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(ethylaminocarbonyl)methanesulfonamide 519172-33-9P,
N-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]succinamic acid 519172-37-3P,
N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]acetyl]methanesulfonamide 519172-45-3P,
3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]propionic acid 519172-49-7P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethyl]amino]pyridine-3-carbonyl]amino]acetic acid 519172-55-5P,
2-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]sulfanyl]-2-methylpropionic acid 519172-59-9P,
2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonyl]-2-methylpropionic acid 519172-62-4P,
[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonyl]acetic acid 519172-65-7P,
N-[3-[3-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-6-methylpyridin-2-yl]propionyl]methanesulfonamide
519172-70-4P, 2-Amino-3-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-

dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionic acid 519172-73-7P,
[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl](methyl)amino]acetic acid 519172-75-9P,
2-[4-Chloro-2-(2H-tetrazol-5-ylmethoxy)phenoxy]-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 519172-77-1P,
2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]nicotinic acid hydrochloride 519172-78-2P,
[2-[2-[(2R)-2-Carbamoylmethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]-5-chlorophenoxy]acetic acid 519172-86-2P,
(4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-1-methylpyrrolidine-(2S)-2-carboxylic acid dihydrochloride 519172-87-3P, C-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(methoxycarbonyl)methanesulfonamide 519172-88-4P, 6-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxymethyl]nicotinic acid 519172-90-8P,
5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-5-oxopentanoic acid 519172-94-2P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]dihydrofuran-2-one 519172-96-4P, 4-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]amino]butyric acid 519172-97-5P, 4-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]amino]butyric acid acetate 519173-03-6P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]amino]acetic acid acetate 519173-07-0P 519173-10-5P,
1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-2-(1H-tetrazol-5-yl)ethanone hydrochloride 519173-13-8P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-3-(1H-tetrazol-5-yl)propan-1-one hydrochloride 519173-14-9P 519173-15-0P, N-[[2-[3-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methoxyphenoxy]acetyl]methanesulfonamide 519173-16-1P,
[5-Chloro-2-[3-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]phenoxy]acetic acid 519173-17-2P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]oxoacetic acid 519173-18-3P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-19-4P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-20-7P,
[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-21-8P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-22-9P, [5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-23-0P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-24-1P,
N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-25-2P,
N-[[5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-26-3P,
2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-27-4P,
4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-28-5P, 6-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyridine-2-carboxylic acid 519173-29-6P,
[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-30-9P, (2R)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-

oxoethoxy]phenoxy]butyric acid 519173-31-0P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-32-1P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-33-2P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-34-3P, (2S)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-35-4P, 2-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-36-5P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-37-6P, 2-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-38-7P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-39-8P, (2S)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-40-1P, (2S)-2-Amino-4-[5-bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-41-2P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyridine-2-carboxylic acid 519173-42-3P, N-[(2R)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyryl]methanesulfonamide 519173-43-4P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methylthiazole-4-carboxylic acid 519173-44-5P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methylfuran-2-carboxylic acid 519173-45-6P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methylfuran-2-carboxylic acid 519173-46-7P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methylthiophene-2-carboxylic acid 519173-47-8P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methylfuran-3-carboxylic acid 519173-48-9P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methylthiophene-2-carboxylic acid 519173-49-0P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methylfuran-2-carboxylic acid 519173-50-3P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methylfuran-2-carboxylic acid 519173-51-4P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-5-(2-methoxyethyl)pyrimidine-2,4,6-trione 519173-53-6P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-5-methylpyrimidine-2,4,6-trione 519173-55-8P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-5-ethylpyrimidine-2,4,6-trione 519173-58-1P, (2R)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid 519173-60-5P, (2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid 519173-62-7P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-2-carboxylic acid 519173-63-8P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2,2-dimethylpropionic acid 519173-65-0P, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-67-2P, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-69-4P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-70-7P, N-[(4S)-4-[5-Chloro-2-[2-[4-(4-

fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenoxy]pyrrolidine - (2S) -2-carbonyl]methanesulfonamide
519173-72-9P, [3-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]ureido]acetic acid
519173-73-0P, 3-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]ureido]propionic acid
519173-74-1P, 3-[3-[4-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]ureido]propionic acid
519173-75-2P, [3-[4-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]ureido]acetic acid
519173-76-3P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl] -3-(methylsulfonyl)urea
519173-77-4P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]benzyl]sulfamoyl]acetic acid
519173-78-5P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]benzyl] -3-(methylsulfonyl)urea
519173-79-6P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]benzyl] -3-(2-methylbenzoyl)sulfamide
519173-80-9P, [[[5-Bromo-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]benzylidene]amino]oxy]acetic acid
519173-81-0P, [[[1-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]ethylidene]amino]oxy]acetic acid
519173-82-1P, [[[1-[5-Bromo-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]ethylidene]amino]oxy]acetic acid
519173-83-2P, [[[[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]methylene]amino]oxy]acetic acid
519173-84-3P, [[[2-[2-[4-(4-Fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy] -5-methylbenzylidene]amino]oxy]acetic acid
519173-85-4P, (2S) -2-[[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]benzyl]oxy]propionic acid
519173-86-5P, (2R) -2-[[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]benzyl]oxy]propionic acid
519173-87-6P, 2-[[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]benzyl]oxy] -2-methylpropionic acid
519173-88-7P, Methylsulfonylcarbamic acid 5-chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]benzyl ester
519173-89-8P, N-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]benzoyl]methanesulfonamide
519173-90-1P, N-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy]benzoyl]methanesulfonamide 519173-91-2P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519173-92-3P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519173-93-4P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]acetyl] -C,C,C-trifluoromethanesulfonamide
519173-94-5P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]acetyl] -4-fluorobenzenesulfonamide 519173-95-6P, N-[[2-[2-[4-(4-Fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy] -4-methoxyphenyl]acetyl]methanesulfonamide 519173-96-7P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]acetyl]benzenesulfonamide 519173-97-8P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]acetyl] -2-methylbenzenesulfonamide 519173-98-9P, Ethanesulfonic acid [[5-chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]acetyl]amide 519173-99-0P, 3,5-Dimethylisoxazole-4-sulfonic acid [[5-chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]acetyl]amide
519174-00-6P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]acetyl]piperazin-1-yl] -2-

oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-01-7P,
 N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-02-8P,
 N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-03-9P,
 N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]-4-methoxybenzenesulfonamide 519174-04-0P,
 2-Chloro-N-[[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]benzenesulfonamide 519174-05-1P,
 N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]-2-fluorobenzenesulfonamide 519174-06-2P,
 N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]-4-methylbenzenesulfonamide 519174-07-3P
 , Propane-2-sulfonic acid [[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]amide 519174-08-4P,
 Propane-1-sulfonic acid [[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]amide 519174-10-8P,
 [4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-cyanoacetamide 519174-11-9P,
 N-[[4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-12-0P,
 N-[[4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-13-1P,
 N-[[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-14-2P,
 N-[[5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-15-3P,
 N-[[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-16-4P,
 N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]phenylmethanesulfonamide 519174-17-5P,
 N-[3-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide 519174-18-6P,
 N-[[5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-19-7P,
 N-[[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-20-0P,
 N-[[5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-21-1P,
 N-[[5-Bromo-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-22-2P,
 N-[[2-[2-[(2R)-2-Ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]acetyl]methanesulfonamide 519174-23-3P,
 N-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide 519174-24-4P,
 N-[3-[2-[2-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]propionyl]methanesulfonamide 519174-25-5P,
 N-[3-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]propionyl]methanesulfonamide 519174-26-6P,
 N-[3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide 519174-27-7P,
 N-[3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide 519174-28-8P,
 N-[3-[2-[2-[(2R)-2-Ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]propionyl]methanesulfonamide 519174-29-9P,
 [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]amino]acetic acid 519174-30-2P,
 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid 519174-31-3P,
 3-[2-[2-[4-(4-Fluorobenzyl)-

(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]acrylic acid 519174-32-4P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid 519174-33-5P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid 519174-34-6P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-[(ethylamino)carbonyl]benzenesulfonamide 519174-35-7P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-[(phenylamino)carbonyl]benzenesulfonamide 519174-36-8P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-[(2-methylphenylamino)carbonyl]benzenesulfonamide 519174-37-9P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-[(4-fluorophenylamino)carbonyl]benzenesulfonamide 519174-38-0P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-(methoxycarbonyl)benzenesulfonamide 519174-39-1P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-(ethoxycarbonyl)benzenesulfonamide 519174-40-4P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-isobutyrylbenzenesulfonamide 519174-41-5P, 5-Chloro-N-cyclopropanecarbonyl-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonamide 519174-42-6P, N-Acetyl-5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonamide 519174-43-7P, 5-Chloro-N-cyclopentanecarbonyl-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonamide 519174-44-8P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonyl]amino]oxoacetic acid 519174-45-9P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-hydroxyacetylbenzenesulfonamide 519174-46-0P, N-Acetyl-C-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-47-1P, N-Acetyl-C-[5-chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-48-2P, N-Acetyl-C-[5-chloro-2-[2-[4-(4-chlorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-49-3P, [5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-50-6P, [5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-51-7P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-52-8P, C-[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-cyclopropanecarbonylmethanesulfonamide 519174-53-9P, C-[5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-trifluoroacetylmethanesulfonamide 519174-54-0P, [5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-55-1P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-56-2P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-57-3P, [5-Bromo-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-58-4P, N-Acetyl-C-[5-chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-59-5P, N-Acetyl-C-[5-bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-60-8P, N-Acetyl-C-[5-bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-61-9P, N-Acetyl-C-[5-bromo-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-62-0P, C-[5-Chloro-2-[2-[4-(4-

fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl] -N-(2,2-dimethylpropionyl)methanesulfonamide 519174-63-1P,
 [5-Chloro-2-[2-[4-(3,4-difluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]methanesulfonamide 519174-64-2P 519174-65-3P,
 N-Acetyl-C-[5-chloro-2-[2-[4-(4-chlorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]methanesulfonamide
 519174-66-4P, C-[5-Chloro-2-[2-[4-(4-chlorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl] -N-cyclopropanecarbonylmethanesulfonamide 519174-67-5P,
 C-[5-Chloro-2-[2-[4-(4-chlorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl] -N-trifluoroacetylmethanesulfonamide 519174-68-6P,
 N-Acetyl-C-[5-chloro-2-[2-[4-(3,4-difluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]methanesulfonamide
 519174-69-7P, C-[5-Chloro-2-[2-[4-(3,4-difluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl] -N-cyclopropanecarbonylmethanesulfonamide 519174-70-0P,
 [5-Bromo-2-[2-[4-(4-chlorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy]phenyl]methanesulfonamide 519174-71-1P, N-Acetyl-C-[5-bromo-2-[2-[4-(4-chlorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy]phenyl]methanesulfonamide 519174-72-2P, N-Acetyl-C-[5-bromo-2-[2-[4-(4-chlorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]methanesulfonamide 519174-73-3P, [5-Bromo-2-[2-[4-(4-chlorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]methanesulfonamide 519174-74-4P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl]methanesulfonyl]amino]oxoacetic acid 519174-75-5P,
 C-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl] -N-(1-hydroxycyclopropanecarbonyl)methanesulfonamide
 519174-76-6P, [[[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy]phenyl]methanesulfonyl]amino]oxoacetic acid
 519174-77-7P, C-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl] -N-methoxyacetylmethanesulfonamide 519174-78-8P, N-Acetyl-C-[2-[2-[4-(4-fluorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy] -5-trifluoromethylphenyl]methanesulfonamide 519174-79-9P,
 N-Acetyl-C-[2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy] -5-trifluoromethylphenyl]methanesulfonamide 519174-80-2P,
 [2-[2-[4-(4-Fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy] -5-trifluoromethylphenyl]methanesulfonamide 519174-81-3P,
 [2-[2-[4-(4-Fluorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy] -5-trifluoromethylphenyl]methanesulfonamide 519174-82-4P,
 C-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl] -N-hydroxyacetylmethanesulfonamide 519174-83-5P,
 C-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]phenyl] -N-(3-hydroxy-3-methylbutyryl)methanesulfonamide
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of piperazine derivs. with CCR1 receptor antagonist activity)

IT 7035-10-1P, (5-Chloro-2-methoxyphenyl)methanol 7035-11-2P,
 4-Chloro-2-chloromethyl-1-methoxybenzene 7048-38-6P,
 (5-Chloro-2-methoxyphenyl)acetonitrile 7417-89-2P, (4-Chloro-2-hydroxyphenoxy)acetic acid 7569-62-2P, (5-Chloro-2-methoxyphenyl)acetic acid 24161-38-4P, (5-Chloro-2-hydroxyphenyl)acetic acid 25032-64-8P,
 4-Chlorobut-3-enenitrile 56913-08-7P, (4-Chloro-2-methoxyphenoxy)acetic acid 62903-23-5P, 4-(5-Chloro-2-hydroxyphenyl)-4-oxobutyric acid 66497-42-5P, 3-Hydroxy-6-methylpyridine-2-carboxaldehyde 76322-41-3P,
 (5-Chloro-2-hydroxyphenyl)acetic acid ethyl ester 82020-51-7P,
 5-Chloro-2-methoxybenzenesulfonamide 82020-64-2P, 5-Chloro-2-

hydroxybenzenesulfonamide 100119-68-4P, 4-(5-Chloro-2-hydroxyphenyl)-4-oxobutyric acid ethyl ester 131803-48-0P, 6-Bromomethylnicotinic acid methyl ester 176433-49-1P, 2,5-Dichloropyridine-3-carboxaldehyde 217645-80-2P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzaldehyde 217648-11-8P, 2-Chloro-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 329219-99-0P, 7-Chlorobenzo[1,4]dioxin-2(3H)-one 331729-64-7P, 2-(5-Chloro-2-hydroxybenzyl)isoindole-1,3-dione 364066-89-7P, (S)-2-(4-Fluorobenzylamino)propionic acid methyl ester 364066-90-0P, (2S)-2-[(2R)-(2-tert-Butoxycarbonylamino)propionyl](4-fluorobenzyl)amino]propionic acid methyl ester 364066-91-1P, (3R,6S)-1-(4-Fluorobenzyl)-3,6-dimethylpiperazine-2,5-dione 364066-97-7P, 2-(4-Chloro-2-nitrophenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 364066-98-8P, 2-(2-Amino-4-chlorophenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 364067-02-7P, 2-(2-Aminomethyl-4-chlorophenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 422270-29-9P, (3R)-1-(4-Fluorobenzyl)-3-methylpiperazine 422270-30-2P, 2-Chloro-1-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]ethanone 422270-31-3P, 2-(4-Chloro-2-nitrophenoxy)-1-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]ethanone 422270-32-4P, 2-(2-Amino-4-chlorophenoxy)-1-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]ethanone 478833-41-9P, (2R,5S)-1-(4-Fluorobenzyl)-2,5-dimethylpiperazine 478833-49-7P, 2-(4-Chloro-2-hydroxymethylphenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 478833-52-2P, 2-(4-Chloro-2-chloromethylphenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 478833-90-8P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid ethyl ester 519171-78-9P, 1-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-(2-hydroxy-4-methylphenyl)propan-1-one 519171-79-0P, [2-[3-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methylphenoxy]acetic acid methyl ester 519171-82-5P, 2-(4-Chloro-2-hydroxyphenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 519171-83-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid methyl ester 519171-86-9P, (2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid ethyl ester 519171-88-1P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-4-oxobutyric acid ethyl ester 519171-90-5P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]carbamic acid 4-nitrophenyl ester 519171-91-6P, 3-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid methyl ester 519171-94-9P, 3-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]amino]propionic acid methyl ester 519171-97-2P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]isoindole-1,3-dione 519172-01-1P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]oxy]acetic acid tert-butyl ester 519172-02-2P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]oxy]acetic acid hydrochloride 519172-05-5P, 1-(tert-Butoxycarbonyl)-1-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]sulfamide 519172-08-8P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetic acid 519172-11-3P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid ethyl ester 519172-12-4P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionic acid ethyl ester 519172-13-5P,

3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionic acid 519172-17-9P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonamide 519172-18-0P 519172-19-1P 519172-23-7P, Acetic acid 2-[[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonyl]amino]-1,1-dimethyl-2-oxoethyl ester 519172-25-9P, Thioacetic acid S-(5-chloro-2-methoxybenzyl) ester 519172-26-0P, (5-Chloro-2-methoxyphenyl)methanesulfonic acid 519172-27-1P, (5-Chloro-2-methoxyphenyl)methanesulfonamide 519172-28-2P, (5-Chloro-2-hydroxyphenyl)methanesulfonamide 519172-29-3P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519172-31-7P, Acetic acid 2-[[[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonyl]amino]-1,1-dimethyl-2-oxoethyl ester 519172-34-0P, 1-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-hydroxyethanone 519172-35-1P 519172-36-2P, 2-(3-Amino-5-chloropyridin-2-yloxy)-1-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]ethanone 519172-39-5P, (2,5-Dichloropyridin-3-yl)acetic acid methyl ester 519172-41-9P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]acetic acid methyl ester 519172-43-1P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]acetic acid 519172-46-4P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridine-3-carboxaldehyde 519172-47-5P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]acrylic acid ethyl ester 519172-48-6P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]propionic acid ethyl ester 519172-50-0P, [2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethyl]carbamic acid tert-butyl ester 519172-51-1P, 2-Amino-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 519172-52-2P, 5-Chloro-2-[[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethyl]amino]nicotinic acid methyl ester 519172-53-3P, 5-Chloro-2-[[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethyl]amino]nicotinic acid hydrochloride 519172-54-4P, [[5-Chloro-2-[[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethyl]amino]pyridine-3-carbonyl]amino]acetic acid methyl ester 519172-56-6P, 6-Chloro-3,3-dimethylbenzo[1,4]oxathiin-2-one 519172-58-8P, 2-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]sulfonyl]-2-methylpropionic acid ethyl ester 519172-60-2P 519172-61-3P 519172-63-5P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]sulfonyl]acetic acid methyl ester 519172-64-6P 519172-66-8P, 3-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-6-methylpyridine-2-carboxaldehyde 519172-67-9P, 3-[3-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-6-methylpyridin-2-yl]acrylic acid ethyl ester 519172-68-0P, 3-[3-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-6-methylpyridin-2-yl]propionic acid ethyl ester 519172-69-1P, Sodium 3-[3-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-6-methylpyridin-2-yl]propionate 519172-71-5P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-2-nitropropionic acid ethyl ester 519172-72-6P, 2-Amino-3-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionic acid ethyl ester 519172-74-8P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl](methyl)amino]acetic acid methyl ester 519172-76-0P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetonitrile 519172-79-3P, [2-(4-

Fluorobenzylamino)ethyl]carbamic acid tert-butyl ester 519172-80-6P,
 4-[(2-tert-Butoxycarbonylaminoethyl)(4-fluorobenzyl)amino]but-2-enoic acid
 methyl ester 519172-81-7P, [(2R)-4-(4-Fluorobenzyl)piperazin-2-yl]acetic
 acid methyl ester 519172-82-8P, 2-[(2R)-1-[(4-Chloro-2-
 hydroxyphenoxy)acetyl]-4-(4-fluorobenzyl)piperazin-2-yl]acetamide
 519172-83-9P, [2-[2-[(2R)-2-Carbamoylmethyl-4-(4-fluorobenzyl)piperazin-1-
 yl]-2-oxoethoxy]-5-chlorophenoxy]acetic acid tert-butyl ester
519172-84-0P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-1,2S-
 dicarboxylic acid di-tert-butyl ester **519172-85-1P**,
 (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-
 yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid dihydrochloride
 519172-89-5P, 6-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]nicotinic acid methyl
 ester 519172-91-9P, 5-(5-Chloro-2-hydroxyphenyl)-5-oxopentanoic acid
 ethyl ester 519172-93-1P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-5-oxopentanoic acid ethyl
 ester 519172-98-6P, 2-(5-Chloro-3-nitropyridin-2-yloxy)-1-[4-(4-
 fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 519172-99-7P,
 2-(3-Amino-5-chloropyridin-2-yloxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]ethanone 519173-00-3P, 4-[[5-Chloro-2-[2-[4-(4-
 fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-
 yl]amino]butyric acid ethyl ester 519173-01-4P, [[5-Chloro-2-[2-[4-(4-
 fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-
 yl]amino]acetic acid ethyl ester 519173-04-7P, 2-(4-Chloro-2-
 hydroxyphenoxy)-1-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]ethanone
 519173-05-8P, 2-(4-Chloro-2-cyanatophenoxy)-1-[4-(4-fluorobenzyl)-(2R)-2-
 methylpiperazin-1-yl]ethanone 519173-08-1P, 2-(4-Chloro-2-(isoxazol-5-
 yl)phenoxy)-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-
 yl]ethanone 519173-09-2P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-3-oxopropionitrile
 519173-11-6P, 4-(5-Chloro-2-hydroxyphenyl)-4-oxobutyronitrile
 519173-12-7P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-4-oxobutyronitrile
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation of piperazine derivs. with CCR1 receptor antagonist activity)

IT **519172-86-2P**, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-
 dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-1-methylpyrrolidine-(2S)-2-
 carboxylic acid dihydrochloride **519173-62-7P**,
 (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-
 yl]-2-oxoethoxy]phenoxy]pyrrolidine-2-carboxylic acid **519173-65-0P**
 , (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-
 yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid
519173-67-2P, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-
 methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic
 acid **519173-69-4P**, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-
 (2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-
 carboxylic acid

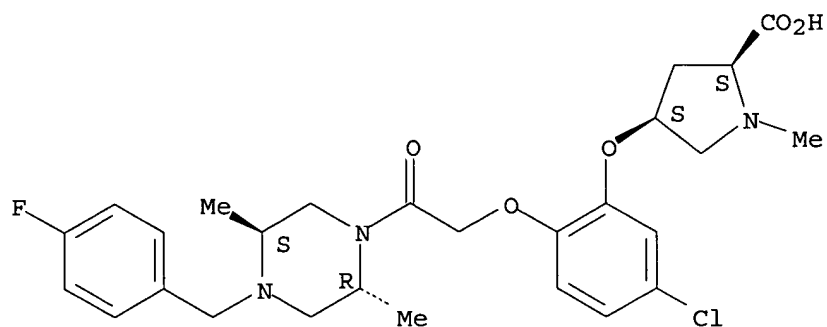
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(drug candidate; preparation of piperazine derivs. with CCR1 receptor
 antagonist activity)

RN 519172-86-2 CAPLUS

CN L-Proline, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-
 dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-1-methyl-, dihydrochloride,
 (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

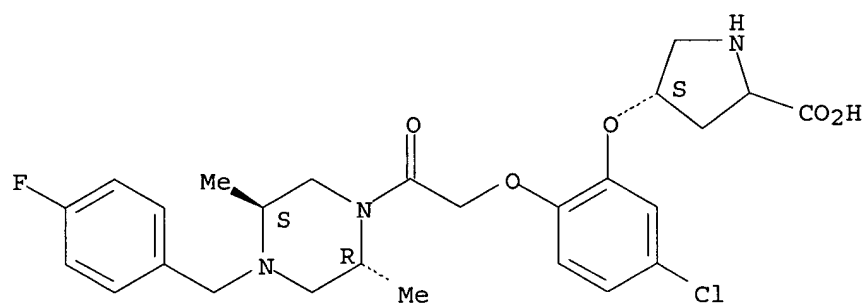


● 2 HCl

RN 519173-62-7 CAPLUS

CN Proline, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, (4S)- (9CI) (CA INDEX NAME)

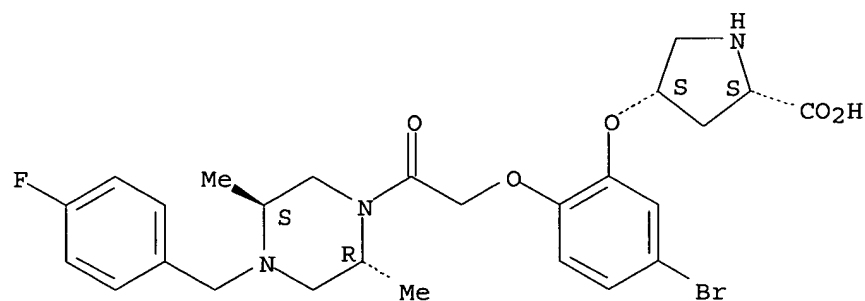
Absolute stereochemistry.



RN 519173-65-0 CAPLUS

CN L-Proline, 4-[5-bromo-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

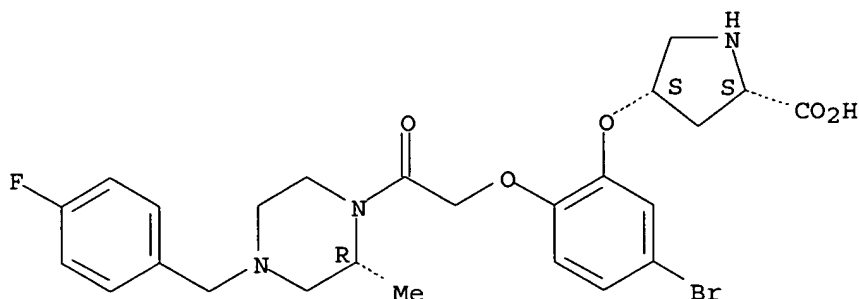


RN 519173-67-2 CAPLUS

CN L-Proline, 4-[5-bromo-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2-methyl-1-

piperazinyll]-2-oxoethoxy]phenoxy]-, (4S)- (9CI) (CA INDEX NAME)

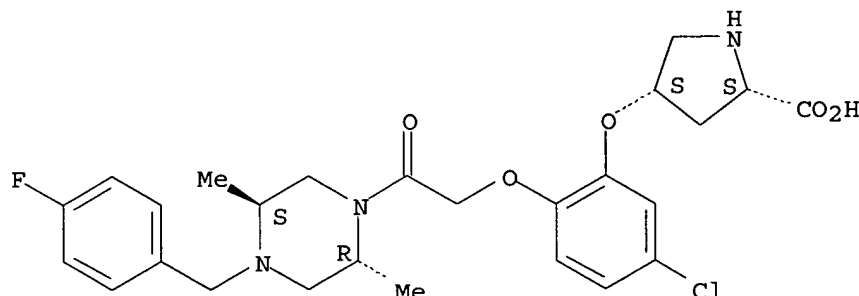
Absolute stereochemistry.



RN 519173-69-4 CAPLUS

CN L-Proline, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyll]-2-oxoethoxy]phenoxy]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

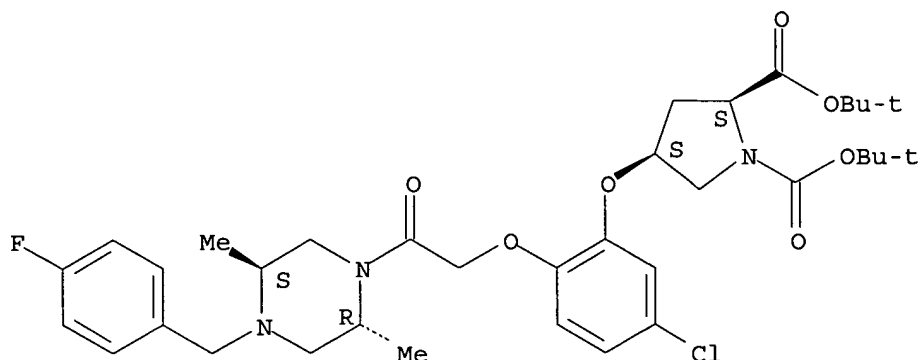


IT 519172-84-0P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-1,2S-dicarboxylic acid di-tert-butyl ester 519172-85-1P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid dihydrochloride
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of piperazine derivs. with CCR1 receptor antagonist activity)

RN 519172-84-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyll]-2-oxoethoxy]phenoxy]-, bis(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

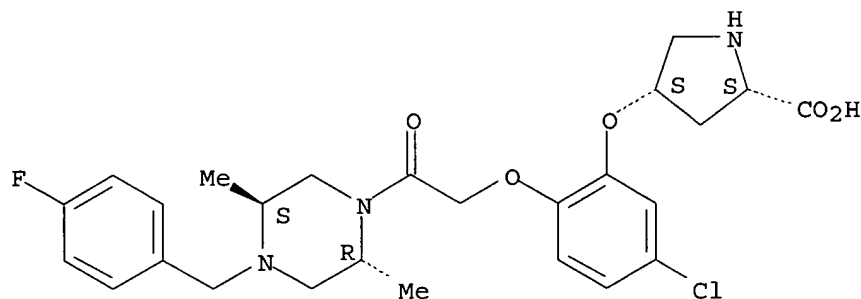
Absolute stereochemistry.



RN 519172-85-1 CAPLUS

CN L-Proline, 4-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenoxy]-, dihydrochloride, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 21 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:215726 CAPLUS

DOCUMENT NUMBER: 139:69229

TITLE: Design and Synthesis of Potent, Non-peptide Inhibitors of HCV NS3 Protease

AUTHOR(S): Zhang, Xiaojun; Schmitt, Aaron C.; Jiang, Wen; Wasserman, Zelda; Decicco, Carl P.

CORPORATE SOURCE: Bristol-Myers Squibb, Discovery Chemistry, Wilmington, DE, 19880, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(6), 1157-1160

CODEN: BMCLE8; ISSN: 0960-894X

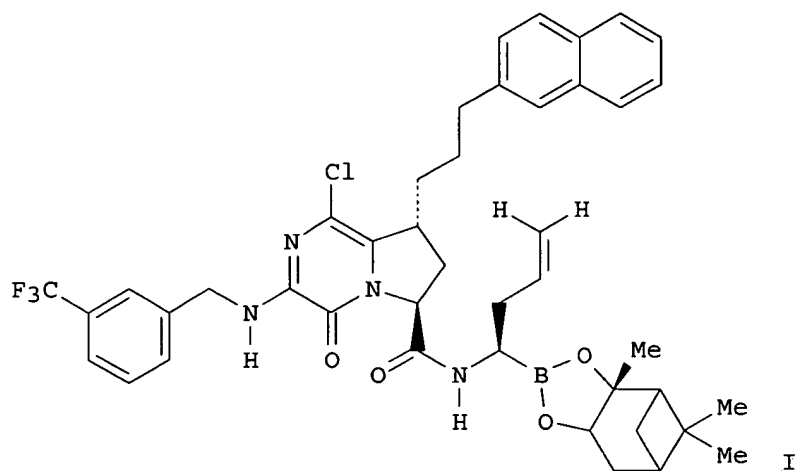
PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:69229

GI



AB Starting from a hexapeptide boronic acid lead, 3-amino bicyclic pyrazinones as novel β -sheet dipeptide mimetics have been designed and synthesized. Side-chain manipulation of this scaffold generated a series of potent, nonpeptidic inhibitors, e.g., I, of HCV NS3 protease.

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 7

IT 153080-85-4P 153080-86-5P 194594-24-6P 284024-88-0P 359028-86-7P
 359028-90-3P 359028-91-4P 464173-85-1P **550375-45-6P**
 550375-46-7P 550375-47-8P 550375-48-9P 550375-49-0P 550375-50-3P
550375-51-4P 550375-52-5P 550375-53-6P 550375-54-7P
 550375-55-8P 550375-56-9P 550375-57-0P 550375-58-1P 550375-59-2P
 550375-60-5P 550375-61-6P 550375-62-7P 550375-63-8P 550375-64-9P
 550375-65-0P 550375-66-1P 550375-67-2P 550375-68-3P 550375-69-4P
 550375-70-7P 550375-71-8P 550375-72-9P 550375-73-0P 550375-74-1P
 550375-75-2P 550375-76-3P 550375-77-4P 550375-78-5P 550375-79-6P
 550375-80-9P 550375-81-0P 550375-82-1P 550376-02-8P 550376-03-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(stereoselective preparation of pyrrolidinopyrazinones via alkylation of N-boc-pyroglytamate followed by reduction/methylation, substitution with cyanide, deprotection, heterocyclization with oxalyl chloride, and substitution with amines)

IT **550375-45-6P 550375-51-4P**

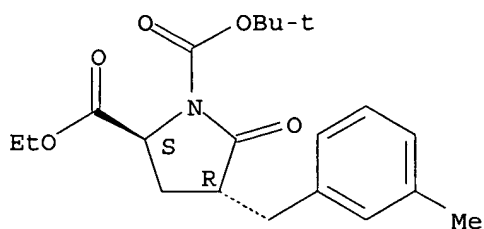
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(stereoselective preparation of pyrrolidinopyrazinones via alkylation of N-boc-pyroglytamate followed by reduction/methylation, substitution with cyanide, deprotection, heterocyclization with oxalyl chloride, and substitution with amines)

RN 550375-45-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-methylphenyl)methyl]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

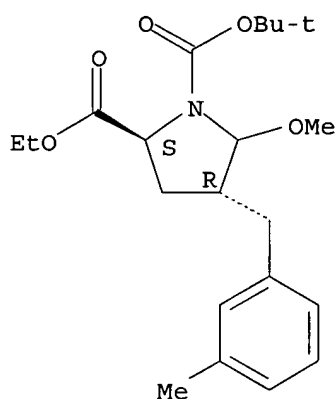
Absolute stereochemistry.



RN 550375-51-4 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 5-methoxy-4-[(3-methylphenyl)methyl]-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 22 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:655594 CAPLUS

DOCUMENT NUMBER: 137:332741

TITLE: 4-Substituted D-Glutamic Acid Analogues: The First Potent Inhibitors of Glutamate Racemase (MurI) Enzyme with Antibacterial Activity

AUTHOR(S): de Dios, Alfonso; Prieto, Lourdes; Martin, Jose Alfredo; Rubio, Almudena; Ezquerra, Jesus; Tebbe, Mark; Lopez de Uralde, Beatriz; Martin, Justina; Sanchez, Ana; LeTourneau, Deborah L.; McGee, James E.; Boylan, Carole; Parr, Thomas R., Jr.; Smith, Michele C.

CORPORATE SOURCE: Eli Lilly and Co., Lilly S.A., Alcobendas, Madrid, 28108, Spain

SOURCE: Journal of Medicinal Chemistry (2002), 45(20), 4559-4570

CODEN: JMCMAR; ISSN: 0022-2623

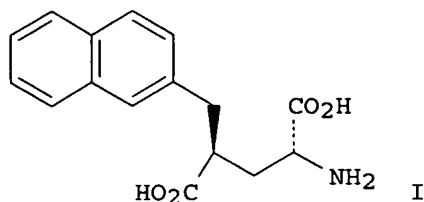
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:332741

GI



AB The first potent inhibitors of glutamate racemase (MurI) enzyme that show whole cell antibacterial activity are described. Optically pure 4-substituted D-glutamic acid analogs with (2R,4S) stereochem. and bearing aryl-, heteroaryl-, cinnamyl-, or biaryl-Me substituents represent a novel class of glutamate racemase inhibitors. Exploration of the D-Glu core led to the identification of lead compds. 2-Naphthylmethyl derivative (I) was a potent competitive inhibitor of glutamate racemase activity ($K_i = 16$ nM, CD assay; $IC_{50} = 0.1$ μ g/mL high-performance liquid chromatog. (HPLC) assay). Thorough structure-activity relation (SAR) studies led to benzothienyl derivs. such as 69 and 74 with increased potency ($IC_{50} = 0.036$ and 0.01 μ g/mL, resp., HPLC assay). These compds. showed potent whole cell antibacterial activity against *S. pneumoniae* PN-R6, and good correlation with the enzyme assay. Some of the prepared substances showed efficacy in an in vivo murine thigh infection model against *Streptococcus pneumoniae*. Data described herein suggest that glutamate racemase may be a viable target for developing new antibacterial agents.

CC 1-3 (Pharmacology)

Section cross-reference(s): 25

IT 100-11-8, p-Nitrobenzyl bromide 103-71-9, Phenyl isocyanate, reactions 939-26-4 1196-19-6 3163-27-7 4392-24-9, Cinnamyl bromide 6165-69-1, 3-Thienylboronic acid 10133-20-7 16004-15-2, p-Iodobenzyl bromide 32316-92-0, 2-Naphthylboronic acid 98437-23-1, 2-Benzothienylboronic acid 144978-12-1 144978-35-8 145798-41-0 191669-98-4 400626-28-0 400626-29-1 **400626-34-8** 400626-71-3 474024-83-4 722461-67-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and structure-activity relationship of D-glutamic acid analogs as potent inhibitors of glutamate racemase with antibacterial activity)

IT **400626-15-5P** 400626-22-4P 400626-35-9P 474024-64-1P 474024-65-2P 474024-66-3P **474024-88-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and structure-activity relationship of D-glutamic acid analogs as potent inhibitors of glutamate racemase with antibacterial activity)

IT 400625-61-8P 400625-92-5P **400626-16-6P** 400626-18-8P 400626-23-5P 400626-26-8P 400626-52-0P 400626-53-1P **721959-91-7P** **721959-93-9P** **721959-96-2P** **721959-97-3P** 721960-12-9P **721960-20-9P** **721960-21-0P** **721960-22-1P** 721960-23-2P 721960-28-7P 721960-30-1P 721963-76-4P **721964-58-5P** **721964-59-6P** **721964-60-9P**

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and structure-activity relationship of D-glutamic acid analogs as potent inhibitors of glutamate racemase with antibacterial activity)

IT **400626-34-8**

RL: RCT (Reactant); RACT (Reactant or reagent)

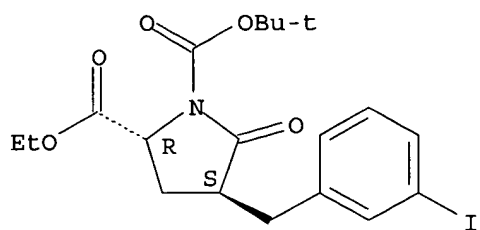
(preparation and structure-activity relationship of D-glutamic acid analogs as potent inhibitors of glutamate racemase with antibacterial activity)

RN 400626-34-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-iodophenyl)methyl]-5-oxo-,

1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 400626-15-5P 474024-88-9P

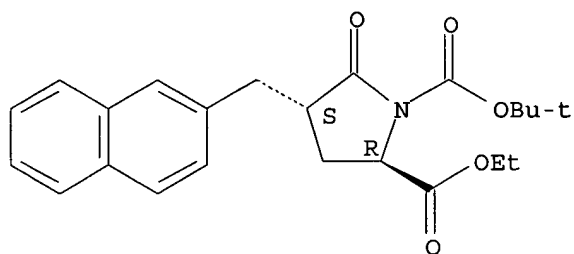
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and structure-activity relationship of D-glutamic acid analogs as potent inhibitors of glutamate racemase with antibacterial activity)

RN 400626-15-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenylmethyl)-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

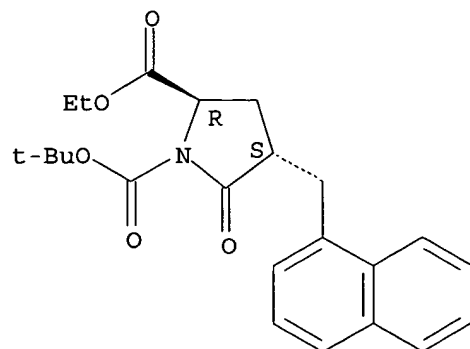
Absolute stereochemistry.



RN 474024-88-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(1-naphthalenylmethyl)-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 400626-16-6P 721959-91-7P 721959-93-9P

721959-96-2P 721959-97-3P 721960-20-9P

721960-21-0P 721960-22-1P 721964-58-5P

721964-59-6P 721964-60-9P

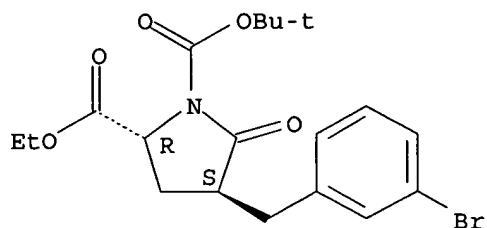
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and structure-activity relationship of D-glutamic acid analogs as potent inhibitors of glutamate racemase with antibacterial activity)

RN 400626-16-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-bromophenyl)methyl]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

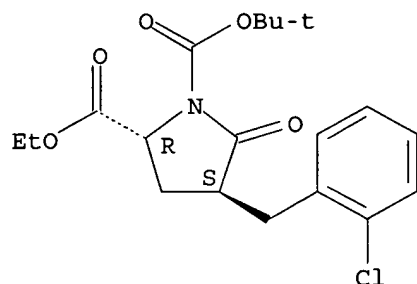
Absolute stereochemistry. Rotation (+).



RN 721959-91-7 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2-chlorophenyl)methyl]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

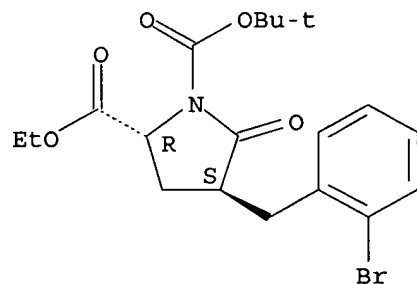
Absolute stereochemistry.



RN 721959-93-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2-bromophenyl)methyl]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

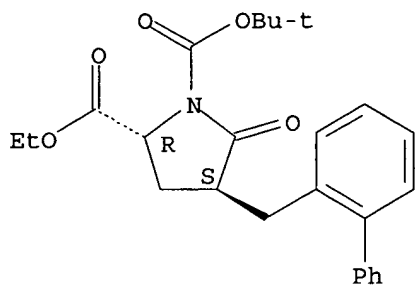
Absolute stereochemistry.



RN 721959-96-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-([1,1'-biphenyl]-2-ylmethyl)-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

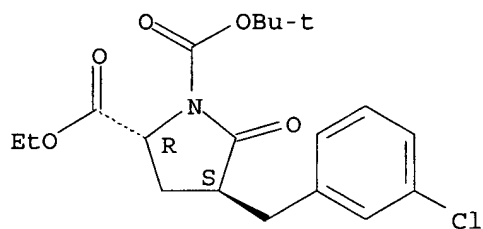
Absolute stereochemistry.



RN 721959-97-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-chlorophenyl)methyl]-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

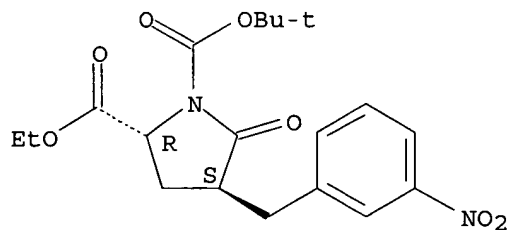
Absolute stereochemistry.



RN 721960-20-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-nitrophenyl)methyl]-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

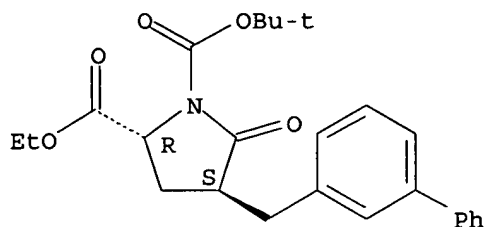
Absolute stereochemistry.



RN 721960-21-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-([1,1'-biphenyl]-3-ylmethyl)-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

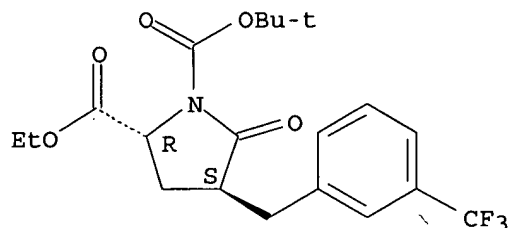
Absolute stereochemistry.



RN 721960-22-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 5-oxo-4-[[3-(trifluoromethyl)phenyl]methyl]-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

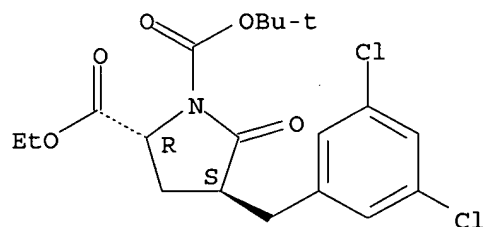
Absolute stereochemistry.



RN 721964-58-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[[3,5-dichlorophenyl]methyl]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

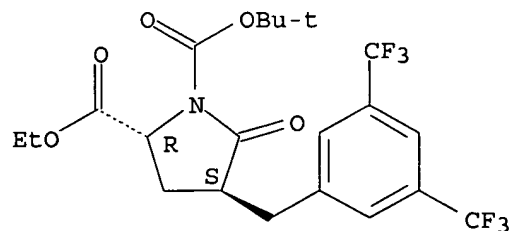
Absolute stereochemistry.



RN 721964-59-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[[3,5-bis(trifluoromethyl)phenyl]methyl]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

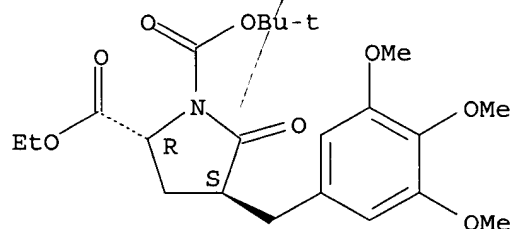
Absolute stereochemistry.



RN 721964-60-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 5-oxo-4-[(3,4,5-trimethoxyphenyl)methyl]-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 23 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:521702 CAPLUS

DOCUMENT NUMBER: 137:93763

TITLE: Preparation of chiral pyrrolidine derivatives as VLA-4 inhibitors

INVENTOR(S): Nakayama, Atsushi; Machinaga, Nobuo; Yoneda, Yoshiyuki; Sugimoto, Yuichi; Chiba, Jun; Watanabe, Toshiyuki; Iimura, Shin

PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 737 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053534	A1	20020711	WO 2001-JP11641	20011228
WO 2002053534	C1	20020919		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2430978	AA	20020711	CA 2001-2430978	20011228
EP 1346982	A1	20030924	EP 2001-272548	20011228
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BR 2001016608	A	20040629	BR 2001-16608	20011228
ZA 2003004059	A	20040706	ZA 2003-4059	20011228
NO 2003002994	A	20030827	NO 2003-2994	20030627
US 2004110945	A1	20040610	US 2003-451159	20030630
PRIORITY APPLN. INFO.:				
			JP 2000-402890	A 20001228
			JP 2001-149923	A 20010518
			WO 2001-JP11641	W 20011228

OTHER SOURCE(S): MARPAT 137:93763
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [WRXM; W = WAA1WB; WA = optionally substituted aryl; A1 = NR1, single bond, C(O); WB = is optionally substituted arylene; R = single bond, NH, OCH2, alkenylene; X = C(O), CH2; M = group represented by the general formula I; R11, R12, R13 each independently = hydrogen, hydroxyl, amino, halogeno; R14 = hydrogen, alkyl; Y = CH2O; Z = optionally substituted arylene; A2 = single bond; R10 = hydroxyl, alkoxy; Q = CH2, S, O, NH], salts thereof, and medicines containing the same are prepared as VLA-4 inhibitors. Title compds. or salts selectively inhibit the binding of cell adhesion mols. to VLA-4 and exhibit high oral absorbability, thus being useful as preventive and/or therapeutic drugs for inflammatory diseases, autoimmune diseases, ~~cancerous metastasis, bronchial asthma, nasal occlusion, diabetes, inflammatory enteric disease, arthritis, etc.~~ The Title compound II was prepared from Et 4-amino-3-chlorophenylacetate, indoline, and Me [(4S)-fluoro-(2S)-pyrrolidinylmethoxy]cyclohexylcarbonate and the title compound III was prepared from Me 3-hydroxy-4-nitrophenylacetate, Ph isothiocyanate, and Me 4-[(4S)-fluoro-(2S)-pyrrolidinylmethoxy]benzoate.

IC ICM C07D209-42

ICS C07D263-58; C07D401-12; C07D401-14; C07D403-06; C07D403-12;
C07D413-12; C07D413-14; C07D417-06; C07D417-12; C07D471-04;
C07D491-056; A61K031-404; A61K031-423; A61K031-428; A61K031-4439;
A61K031-496; A61K031-454; A61K031-4725; A61K031-416

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 27, 63

IT 399-97-3P 2516-40-7P 2835-97-4P 3507-17-3P 3622-19-3P 3622-40-0P
4494-18-2P, 1-Isoquinolinecarboxaldehyde 4498-67-3P,
1H-Indazole-3-carboxylic acid 20357-15-7P 27018-76-4P 27257-15-4P
28691-47-6P, 1,2-Benzisoxazole-3-carboxylic acid 30095-98-8P
31912-02-4P 34252-44-3P 42113-13-3P, Methyl (3-methyl-4-
hydroxy)benzoate 43120-28-1P 50264-71-6P 50890-83-0P 56850-94-3P
57764-49-5P 59184-90-6P 61873-93-6P 66684-61-5P 72925-16-7P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of chiral pyrrolidine derivs. as VLA-4 inhibitors)

IT 317357-41-8P 317357-42-9P

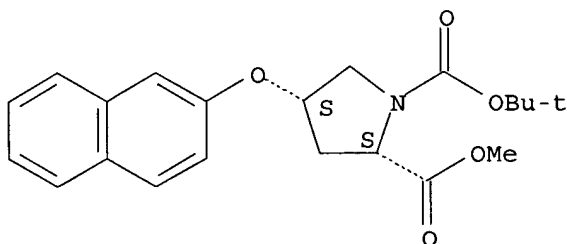
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of chiral pyrrolidine derivs. as VLA-4 inhibitors)

RN 317357-41-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

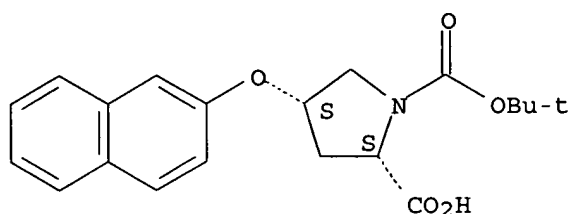
Absolute stereochemistry.



RN 317357-42-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-, 1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 143 THERE ARE 143 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 24 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:487555 CAPLUS

DOCUMENT NUMBER: 137:47220

TITLE: Preparation of substituted pyrrolidines as CCR-3 receptor antagonists

INVENTOR(S): Kertesz, Denis John; Roepel, Michael Garret

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.

SOURCE: PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

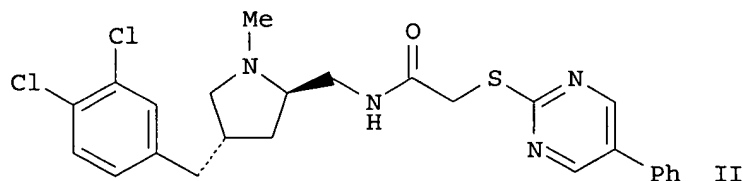
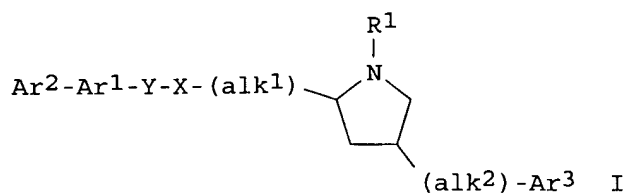
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002050064	A1	20020627	WO 2001-EP14670	20011213
W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
RW:			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG	
CA 2431767	AA	20020627	CA 2001-2431767	20011213
AU 2002016107	A5	20020701	AU 2002-16107	20011213
EP 1358181	A1	20031105	EP 2001-271370	20011213
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR	
BR 2001016352	A	20031202	BR 2001-16352	20011213
JP 2004519443	T2	20040702	JP 2002-551560	20011213
US 2002198255	A1	20021226	US 2001-34034	20011219
US 6552028	B2	20030422		
US 2003199532	A1	20031023	US 2003-368097	20030218
ZA 2003004530	A	20040910	ZA 2003-4530	20030610
PRIORITY APPLN. INFO.:			US 2000-256585P	P 20001219
			WO 2001-EP14670	W 20011213
			US 2001-34034	A3 20011219

OTHER SOURCE(S): MARPAT 137:47220

GI



AB The title compds. [I; R1 = H, C1-6 alkyl, acyl, heteroalkyl, -CONR3R4 (where R3, R4 = H, C1-6 alkyl), -CO2R5 (where R5 = H, C1-6 alkyl, heteroalkyl), SO2R6 (where R6 = C1-6 alkyl); alk1 = C1-6 alkylene; X = NHCO, CONH; Y = C1-3 alkylene, C2-3 alkylene wherein one of the carbon atoms is replaced by a heteroatom selected from the group consisting of O, NRb [where Rb = H, C1-6 alkyl, acyl, CONR7R8 (where R7, R8 = H, C1-6 alkyl), CO2R9 (where R9 = H, C1-6 alkyl, heteroalkyl), aryl, aryl C1-6 alkyl] and S(O)n (wherein n is an integer from 0 to 2); Ar1 = a heteroaryl group or Ph wherein the heteroaryl or Ph group is substituted, in addition to the Ar2 group, with a group selected from the group consisting of H, halo, C1-6 alkyl, C1-6 alkoxy, NO2, amido, aminosulfonyl and sulfonylamino; Ar2 = aryl; alk2 = C1-6 alkylene wherein one of the carbon atoms is optionally replaced by CO, NRc [where Rc = H, C1-6 alkyl, acyl, -CONR10R11 (where R11, R12 = H, C1-6 alkyl), CO2R12 (where R12 = H, C1-6 alkyl, heteroalkyl), aryl, aryl C1-6 alkyl] or S(O)n1 (wherein n1 is an integer from 0 to 2); Ar3 = C3-7 cycloalkyl, aryl, heteroaryl] or pharmaceutically acceptable salts thereof are prepared. The compds. are useful as CCR-3 receptor antagonists and, therefore, may be used for the treatment of diseases treatable by administration of a CCR-3 receptor antagonists, e.g. asthma. Thus, to a solution of (2R,4S)-2-aminomethyl-3-(3,4-dichlorobenzyl)-1-methylpyrrolidine (24 mg, 0.088 mmol) in CH2Cl2 (5 mL) was added 5-phenylpyrimidin-2-ylthioacetic acid (24 mg, 0.097 mmol), EDCI (21 mg, 0.11 mmol) and HOBT (1 mg, 0.009 mmol) and the reaction mixture was stirred for 2 h at room temperature to give, after workup, N-[2-[(2R,4S)-4-(3,4-dichlorobenzyl)-1-methylpyrrolidin-2-yl]methyl]-2-[(5-phenylpyrimidin-2-yl)thio]acetamide (II). II showed IC50 of 0.028 μ M for inhibiting the binding of [125I]eotaxin to CCR-3 L1.2 transfectant cells.

IC ICM C07D403-12

ICS C07D239-38; A61K031-506; A61P011-06

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT 144978-12-1P **438494-67-8P** 438494-69-0P, (2S,4R)-4-(3,4-Dichlorobenzyl)-1-tert-butoxycarbonyl-2-(hydroxymethyl)pyrrolidine 438494-71-4P, (2S,4R)-4-(3,4-Dichlorobenzyl)-1-tert-butoxycarbonyl-2-(methanesulfonyloxymethyl)pyrrolidine 438494-72-5P, (2S,4R)-2-(Cyanomethyl)-4-(3,4-dichlorobenzyl)-1-tert-butoxycarbonylpyrrolidine 438494-73-6P, (2S,4R)-2-(2-Aminoethyl)-4-(3,4-dichlorobenzyl)-1-tert-butoxycarbonylpyrrolidine 438494-75-8P 438494-76-9P, 5-(3,4-Dimethoxyphenyl)-2-mercaptopyrimidine 438494-77-0P, Ethyl [[5-(3,4-dimethoxyphenyl)pyrimidin-2-yl]thio]acetate 438494-78-1P, [[5-(3,4-Dimethoxyphenyl)pyrimidin-2-yl]thio]acetic acid **438494-82-7P**, Ethyl (5R,3S)-3-(3,4-dichlorobenzyl)-1-(tert-

butoxycarbonyl)-2-oxopyrrolidine-5-carboxylate **438494-83-8P**, Ethyl (3S,5R)-3-(3,4-dichlorobenzyl)-2-oxopyrrolidine-5-carboxylate **438494-84-9P**, Ethyl (3S,5R)-3-(3,4-dichlorobenzyl)-1-methyl-2-oxopyrrolidine-5-carboxylate **438494-85-0P**, Ethyl (3R,5R)-3-(3,4-dichlorobenzyl)-1-methyl-2-oxopyrrolidine-5-carboxylate **438494-86-1P**, (4R,5R)-5-Aminocarbonyl-4-(3,4-dichlorobenzyl)-1-methyl-2-oxopyrrolidine **438494-87-2P**, (2R,4R)-2-Aminomethyl-4-(3,4-dichlorobenzyl)-1-methylpyrrolidine **438494-90-7P**, (3S,5R)-5-Aminocarbonyl-3-(3,4-dichlorobenzyl)-1-methyl-2-oxopyrrolidine **438494-91-8P**, (2R,4S)-2-Aminomethyl-4-(3,4-dichlorobenzyl)-1-methylpyrrolidine **438494-93-0P**, (2S,4R)-2-Hydroxymethyl-4-(3,4-dichlorobenzyl)-1-methylpyrrolidine **438494-94-1P**, (2S,4R)-4-(3,4-dichlorobenzyl)-2-(methanesulfonyloxymethyl)-1-methylpyrrolidine **438494-95-2P**, (2S,4R)-2-Cyanomethyl-4-(3,4-dichlorobenzyl)-1-methylpyrrolidine **438494-96-3P**, (2S,4R)-2-(2-Aminoethyl)-4-(3,4-dichlorobenzyl)-1-methylpyrrolidine **438494-98-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of substituted pyrrolidines as CCR-3 receptor antagonists)

IT **438494-67-8P 438494-82-7P**, Ethyl (5R,3S)-3-(3,4-dichlorobenzyl)-1-(tert-butoxycarbonyl)-2-oxopyrrolidine-5-carboxylate **438494-83-8P**, Ethyl (3S,5R)-3-(3,4-dichlorobenzyl)-2-oxopyrrolidine-5-carboxylate **438494-84-9P**, Ethyl (3S,5R)-3-(3,4-dichlorobenzyl)-1-methyl-2-oxopyrrolidine-5-carboxylate **438494-85-0P**, Ethyl (3R,5R)-3-(3,4-dichlorobenzyl)-1-methyl-2-oxopyrrolidine-5-carboxylate

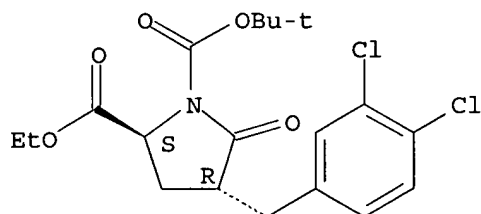
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of substituted pyrrolidines as CCR-3 receptor antagonists)

RN **438494-67-8 CAPLUS**

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3,4-dichlorophenyl)methyl]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

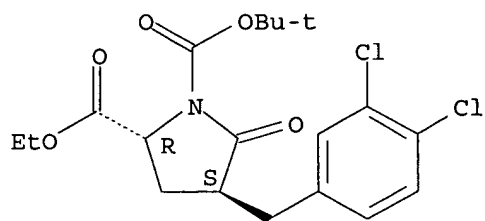
Absolute stereochemistry.



RN **438494-82-7 CAPLUS**

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3,4-dichlorophenyl)methyl]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

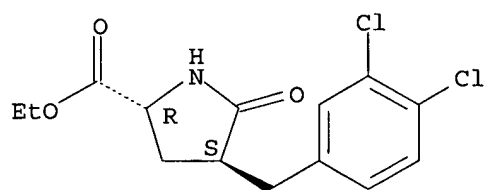
Absolute stereochemistry.



RN 438494-83-8 CAPLUS

CN D-Proline, 4-[(3,4-dichlorophenyl)methyl]-5-oxo-, ethyl ester, (4S)- (9CI)
(CA INDEX NAME)

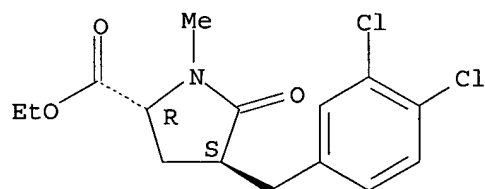
Absolute stereochemistry.



RN 438494-84-9 CAPLUS

CN D-Proline, 4-[(3,4-dichlorophenyl)methyl]-1-methyl-5-oxo-, ethyl ester,
(4S)- (9CI) (CA INDEX NAME)

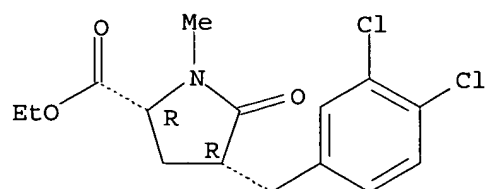
Absolute stereochemistry.



RN 438494-85-0 CAPLUS

CN D-Proline, 4-[(3,4-dichlorophenyl)methyl]-1-methyl-5-oxo-, ethyl ester,
(4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

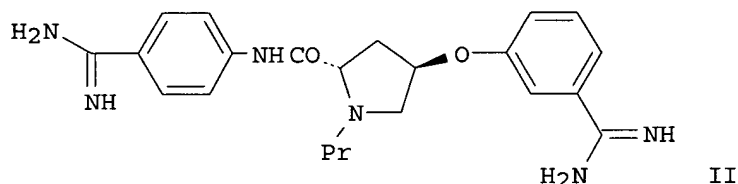
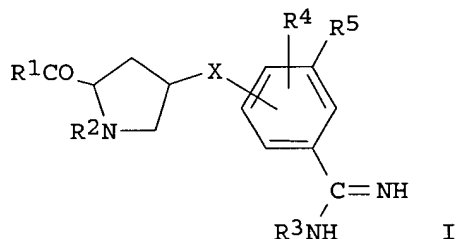
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THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 25 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:220553 CAPLUS
 DOCUMENT NUMBER: 136:263086
 TITLE: Amidine inhibitors of serine proteases
 INVENTOR(S): ~~Pastor, Richard M.~~; Artis, Dean R.; Olivera, Alan G.
 PATENT ASSIGNEE(S): Genentech, Inc., USA
 SOURCE: PCT Int. Appl., 45 pp.
 CODEN: RIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022575	A1	20020321	WO 2001-US27640	20010905
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2421548	AA	20020321	CA 2001-2421548	20010905
AU 2001088819	A5	20020326	AU 2001-88819	20010905
US 2002055469	A1	20020509	US 2001-947424	20010905
US 6410733	B2	20020625		
EP 1317429	A1	20030611	EP 2001-968579	20010905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004509104	T2	20040325	JP 2002-526828	20010905
US 2003229133	A1	20031211	US 2003-363557	20030304
US 6838479	B2	20050104		
PRIORITY APPLN. INFO.:			US 2000-231679P	P 20000911
			WO 2001-US27640	W 20010905
OTHER SOURCE(S):		MARPAT 136:263086		
GI				



AB Pyrrolidinylarylamidines I [X = O, S, (un)substituted CH₂, NH; R₁ = H, (un)substituted OH, NH₂; R₂ = H, (un)substituted aliphatic, cycloaliph.; R₃ = h, protective group; R₄ = H, OH, halogen, amino, NO₂, amidino, guanidino, acylamino, R₅ = H; R₄R₅ = atoms required to complete a carbocyclic or heterocyclic ring] were prepared for use as serine protease inhibitors. In particular, I bind to factor VIIa, tissue factor/factor Xa complex, thrombin, trypsin, plasmin and kallikrein and have anticoagulant activity. Thus, the aminidine II was prepared by solid-supported synthesis and has binding affinities for factor VIIa 7.8, factor Xa 0.297, thrombin 4.744, trypsin 0.866, plasmin 7.36, and kallikrein 6.559 μM.

IC ICM C07D207-16

ICS C07D401-06; C07D403-12; C07D207-48; C07D401-12; A61K031-40; A61K031-401; A61K031-4025; A61P007-02

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT	404908-64-1P	404908-65-2P	404908-66-3P	404908-67-4P	404908-69-6P
	404908-70-9P	404908-71-0P	404908-72-1P	404908-73-2P	404908-74-3P
	404908-75-4P	404908-76-5P	404908-77-6P	404908-78-7P	404908-79-8P
	404908-80-1P	404908-81-2P	404908-83-4P	404908-85-6P	404908-86-7P
	404908-87-8P	404908-89-0P	404908-90-3P	404908-91-4P	
	404908-92-5P	404908-93-6P	404908-94-7P	404908-95-8P	
	404908-96-9P	404908-97-0P	404908-98-1P	404908-99-2P	404909-00-8P
	404909-01-9P	404909-02-0P	404909-03-1P	404909-04-2P	
	404909-05-3P	404909-06-4P	404909-07-5P	404909-08-6P	404909-09-7P
	404909-10-0P	404909-11-1P	404909-12-2P	404909-13-3P	404909-15-5P
	404909-16-6P	404909-17-7P	404909-18-8P	404909-19-9P	404909-20-2P
	404909-21-3P	404909-22-4P	404909-23-5P	404909-24-6P	
	404909-25-7P	404909-26-8P	404909-27-9P	404909-28-0P	
	404909-29-1P	404909-30-4P	404909-31-5P	404909-32-6P	404909-33-7P
	404909-34-8P	404909-35-9P	404909-36-0P	404909-37-1P	
	404909-38-2P	404909-40-6P	404909-41-7P	404909-42-8P	
	404909-43-9P	404909-44-0P	404909-45-1P	404909-46-2P	
	404909-47-3P	404909-48-4P			

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrroldinylbenzamidines as serine protease inhibitors)

IT 24722-35-8DP, 3-Hydroxybenzamidine, polymer-bound 113775-22-7P
 160833-27-2P, 3-tert-Butyldimethylsilyloxybenzonitrile 186320-37-6P
 404909-49-5P, N-Hydroxy-3-tert-butyl dimethylsilyloxybenzamidine
 404909-50-8DP, 3-tert-Butyldimethylsilyloxybenzamidine, polymer-bound
 404909-50-8P, 3-tert-Butyldimethylsilyloxybenzamidine
 404909-51-9DP, polymer-bound 404909-52-0DP,
 polymer-bound 404909-53-1P 404909-54-2P 404909-55-3P
 404909-56-4DP, polymer-bound 404909-57-5DP,
 polymer-bound
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

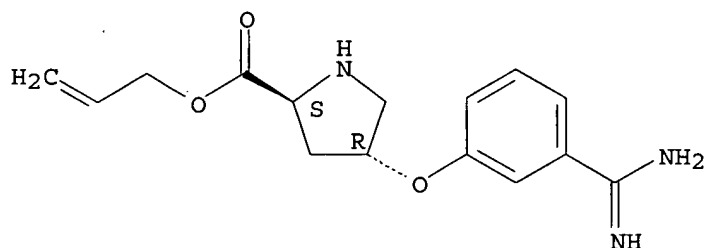
(preparation of pyrroldinylbenzamidines as serine protease inhibitors)

IT 404908-92-5P 404909-01-9P 404909-25-7P
 404909-35-9P 404909-40-6P 404909-42-8P
 404909-44-0P 404909-46-2P 404909-47-3P
 404909-48-4P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of pyrroldinylbenzamidines as serine protease inhibitors)

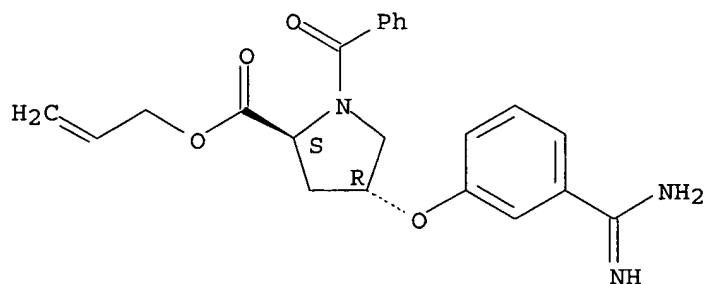
RN 404908-92-5 CAPLUS
 CN L-Proline, 4-[3-(aminoiminomethyl)phenoxy]-, 2-propenyl ester, (4R)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



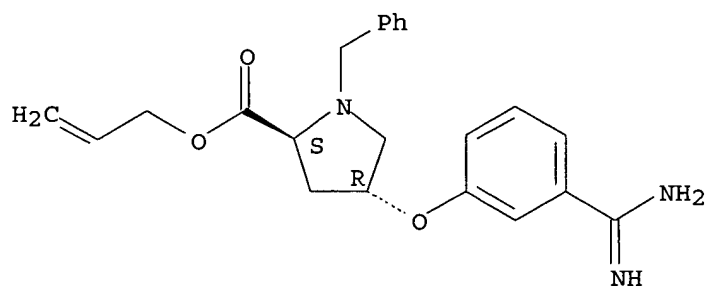
RN 404909-01-9 CAPLUS
 CN L-Proline, 4-[3-(aminoiminomethyl)phenoxy]-1-benzoyl-, 2-propenyl ester,
 (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 404909-25-7 CAPLUS
 CN L-Proline, 4-[3-(aminoiminomethyl)phenoxy]-1-(phenylmethyl)-, 2-propenyl
 ester, (4R)- (9CI) (CA INDEX NAME)

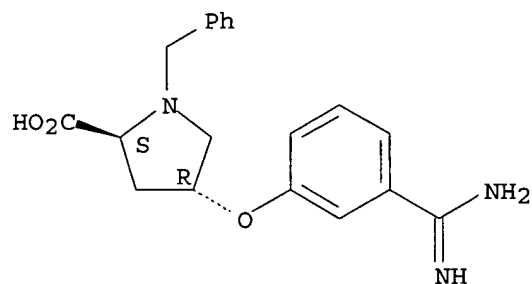
Absolute stereochemistry.



RN 404909-35-9 CAPLUS

CN L-Proline, 4-[3-(aminoiminomethyl)phenoxy]-1-(phenylmethyl)-, (4R)-(9CI)
(CA INDEX NAME)

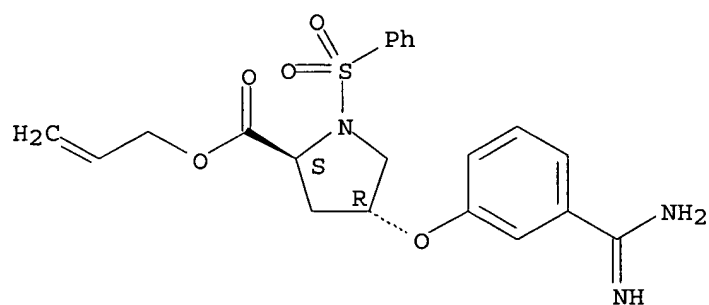
Absolute stereochemistry.



RN 404909-40-6 CAPLUS

CN L-Proline, 4-[3-(aminoiminomethyl)phenoxy]-1-(phenylsulfonyl)-, 2-propenyl ester, (4R)-(9CI) (CA INDEX NAME)

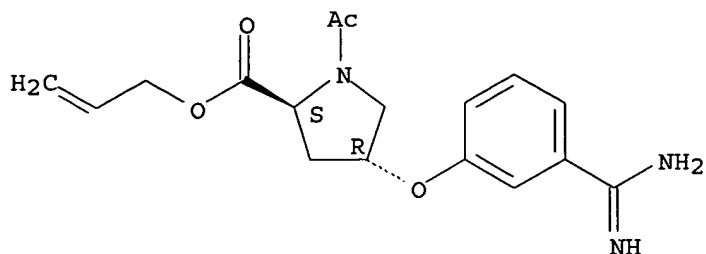
Absolute stereochemistry.



RN 404909-42-8 CAPLUS

CN L-Proline, 1-acetyl-4-[3-(aminoiminomethyl)phenoxy]-, 2-propenyl ester,
(4R)-(9CI) (CA INDEX NAME)

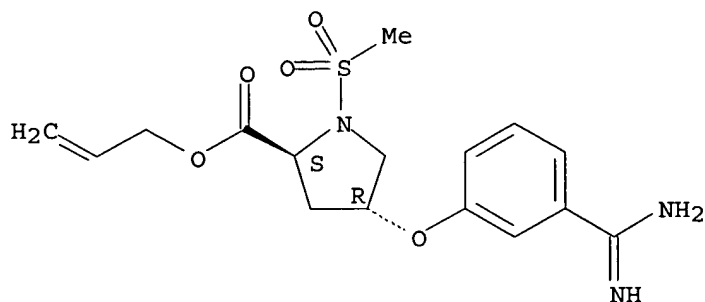
Absolute stereochemistry.



RN 404909-44-0 CAPLUS

CN L-Proline, 4-[3-(aminoiminomethyl)phenoxy]-1-(methylsulfonyl)-, 2-propenyl ester, (4R)- (9CI) (CA INDEX NAME)

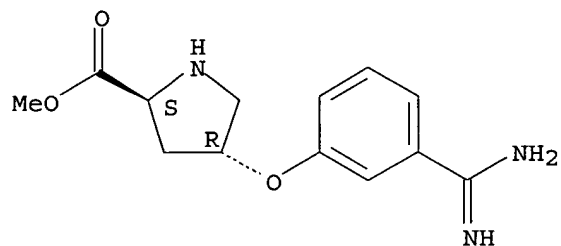
Absolute stereochemistry.



RN 404909-46-2 CAPLUS

CN L-Proline, 4-[3-(aminoiminomethyl)phenoxy]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

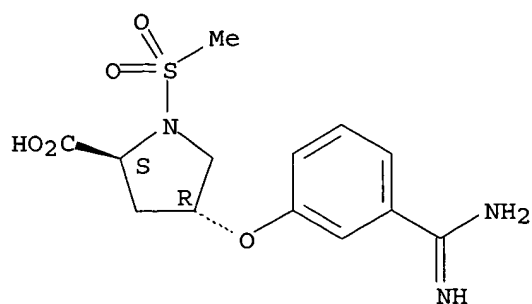
Absolute stereochemistry.



RN 404909-47-3 CAPLUS

CN L-Proline, 4-[3-(aminoiminomethyl)phenoxy]-1-(methylsulfonyl)-, (4R)- (9CI) (CA INDEX NAME)

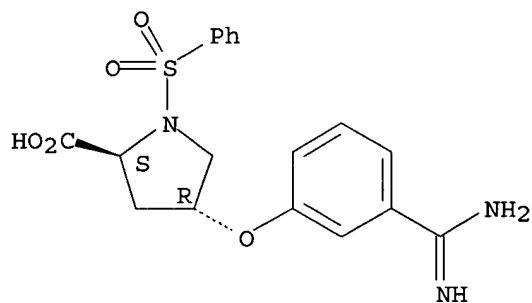
Absolute stereochemistry.



RN 404909-48-4 CAPLUS

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(9CI) (CA INDEX NAME)

Absolute stereochemistry.



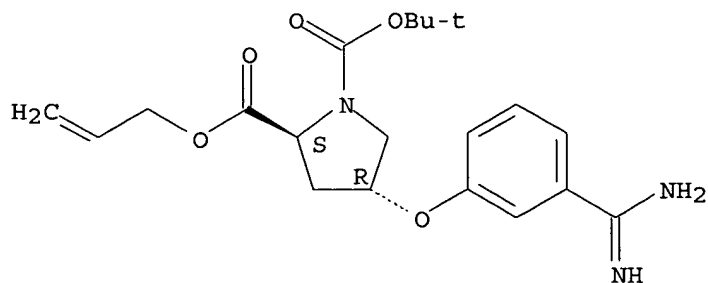
IT 404909-51-9DP, polymer-bound 404909-52-0DP,
polymer-bound 404909-56-4DP, polymer-bound 404909-57-5DP
, polymer-bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of pyrrolidinybenzamidines as serine protease inhibitors)

RN 404909-51-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[3-(aminoiminomethyl)phenoxy]-,
1-(1,1-dimethylethyl) 2-(2-propenyl) ester, (2S,4R)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

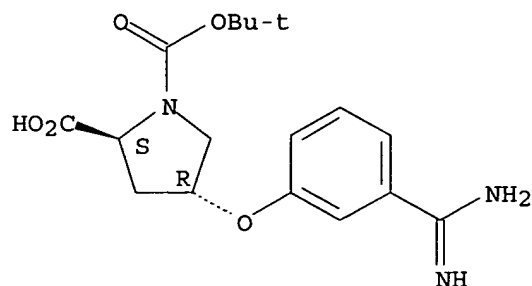


RN 404909-52-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[3-(aminoiminomethyl)phenoxy]-,

1-(1,1-dimethylethyl) ester, (2S,4R) - (9CI) (CA INDEX NAME)

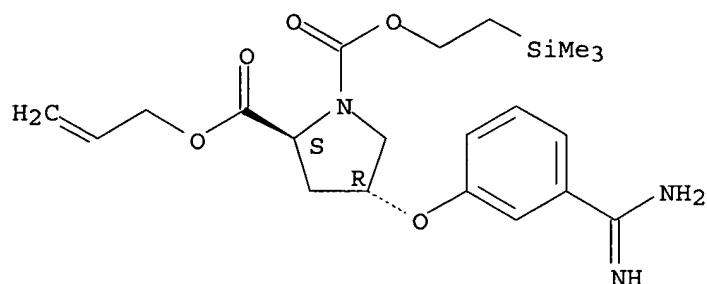
Absolute stereochemistry.



RN 404909-56-4 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[3-(aminoiminomethyl)phenoxy]-, 2-(2-propenyl) 1-[2-(trimethylsilyl)ethyl] ester, (2S,4R) - (9CI) (CA INDEX NAME)

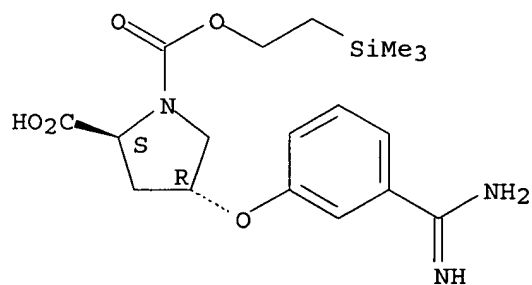
Absolute stereochemistry.



RN 404909-57-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[3-(aminoiminomethyl)phenoxy]-, 1-[2-(trimethylsilyl)ethyl] ester, (2S,4R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 26 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:171852 CAPLUS

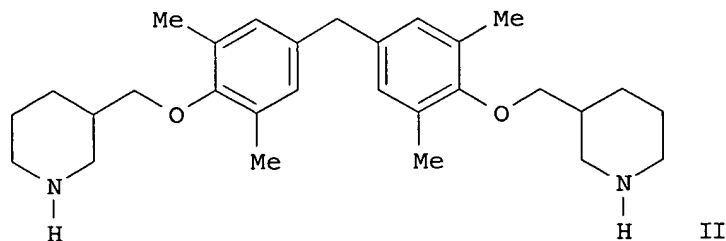
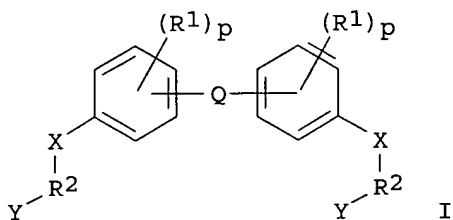
DOCUMENT NUMBER: 136:216528

TITLE: Preparation of linked benzene derivatives as sodium

channel modulators
 INVENTOR(S): Chinn, Jason P.; Choi, Seok-ki; Fatheree, Paul R.;
 Marquess, Daniel; Turner, S. Derek
 PATENT ASSIGNEE(S): Advanced Medicine, Inc., USA
 SOURCE: PCT Int. Appl., 119 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018334	A2	20020307	WO 2001-US27128	20010830
WO 2002018334	A3	20020613		
WO 2002018334	B1	20020926		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001086965	A5	20020313	AU 2001-86965	20010830
US 2003027822	A1	20030206	US 2001-943420	20010830
US 6756400	B2	20040629		
US 2004204460	A1	20041014	US 2004-824738	20040415
PRIORITY APPLN. INFO.:			US 2000-229572P	P 20000831
			US 2001-943420	A3 20010830
			WO 2001-US27128	W 20010830

OTHER SOURCE(S): MARPAT 136:216528
 GI



AB Title compds. I [R1 = alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, etc.; R2 = bond, (un)substituted alkylene; X = O, NRm wherein Rm = H, (un)substituted-alkyl, -alkenyl, -alkynyl, -heteroaryl, etc.; Y = (un)substituted amine or a (un)substituted heterocyclyl containing at least one N, wherein each nitrogen of the heterocyclyl is substituted with R3 or is linked to R2; R3 = H, alkyl, aryl, oxo, heterocyclyl, etc., or R3 is joined to another substituent of Y to form a (un)substituted C1-4 alkylene group; Q = O, S(O)m, (CR5R6)w, O(CR5R6)rO, N(Rk) where m = 0-2, w = 1-3, r = 2-3; Rk = H, (un)substituted alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl or heterocyclyl; R5 and R6 are independently H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; or R5 and R6 together with the carbon atom to which they are attached may form a (un)substituted-cycloalkyl or -heterocyclyl; p = 0-4] and their pharmaceutically acceptable salts are prepared and disclosed as sodium channel modulators. Thus, II was prepared from 4,4'-methylenebis(2,6-dimethylphenol) and N-Boc-3-(hydroxymethyl)piperidine under Mitsunobu conditions with successive N-deprotection. As sodium channel modulators, I are useful for treating diseases or conditions associated with sodium channel activity, such as neuropathic pain. II exhibited an IC50 value of less than 100 μ M in a rat cerebellar granule neuron assay. The invention also provides pharmaceutical compns. comprising a compound of formula (I) or a salt thereof, as well as therapeutic methods comprising administering such a compound or salt to a mammal (e.g. a human).

IC ICM C07D207-00

CC 25-10 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 1, 63

IT 402759-46-0P 402759-47-1P 402759-48-2P 402759-49-3P 402759-51-7P
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 402760-71-8P 402760-72-9P 402760-73-0P 402760-74-1P 402760-75-2P
 402760-76-3P 402760-77-4P 402760-79-6P 402760-81-0P 402760-83-2P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of linked benzene derivs. via Mitsunobu reaction of linked phenols with the requisite alc.)

IT 5731-17-9P 116574-71-1P, N-tert-Butoxycarbonyl-3-(hydroxymethyl)piperidine 402761-15-3P 402761-16-4P 402761-17-5P 402761-18-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of linked benzene derivs. via Mitsunobu reaction of linked phenols with the requisite alc.)

IT 402759-84-6P 402759-90-4P

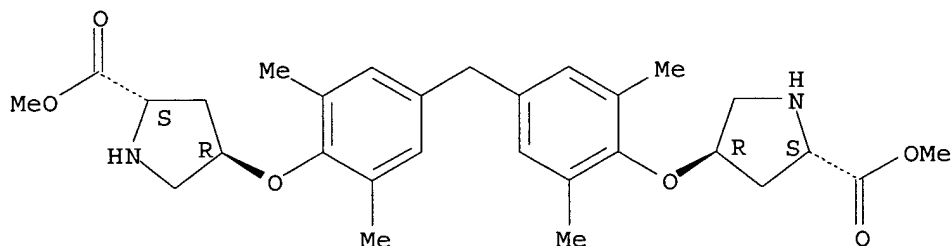
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of linked benzene derivs. via Mitsunobu reaction of linked phenols with the requisite alc.)

RN 402759-84-6 CAPLUS

CN L-Proline, 4,4'-[methylenebis[(2,6-dimethyl-4,1-phenylene)oxy]]bis-, dimethyl ester, (4R,4'R)-(9CI) (CA INDEX NAME)

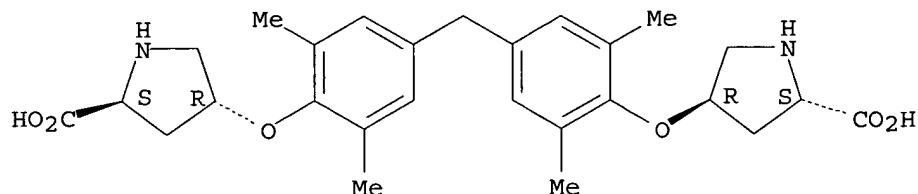
Absolute stereochemistry.



RN 402759-90-4 CAPLUS

CN L-Proline, 4,4'-[methylenebis[(2,6-dimethyl-4,1-phenylene)oxy]]bis-, (4R,4'R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 402761-15-3P 402761-18-6P

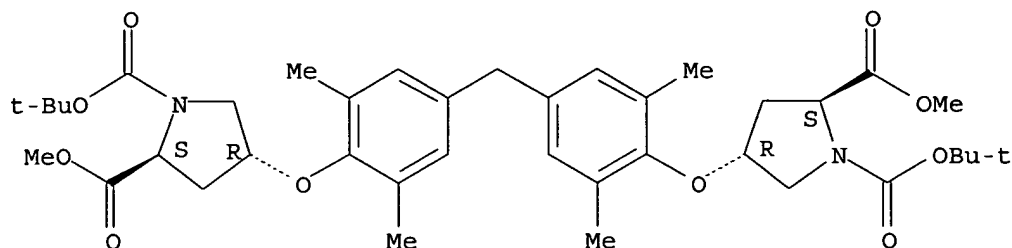
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of linked benzene derivs. via Mitsunobu reaction of linked phenols with the requisite alc.)

RN 402761-15-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4,4'-[methylenebis[(2,6-dimethyl-4,1-phenylene)oxy]]bis-, 1,1'-bis(1,1-dimethylethyl) 2,2'-dimethyl ester, (2S,2'S,4R,4'R)-(9CI) (CA INDEX NAME)

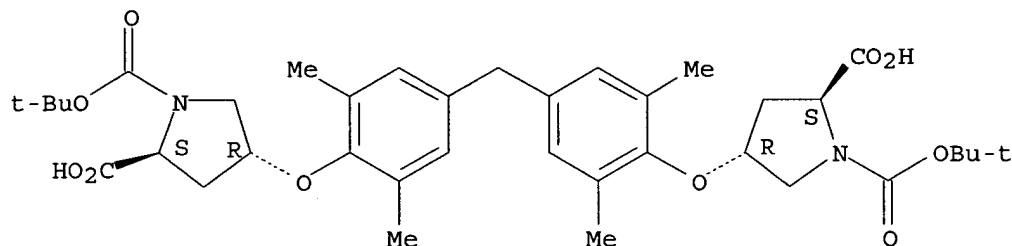
Absolute stereochemistry.



RN 402761-18-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4,4'-[methylenebis[(2,6-dimethyl-4,1-phenylene)oxy]]bis-, 1,1'-bis(1,1-dimethylethyl) ester, (2S,2'S,4R,4'R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 27 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:142656 CAPLUS

DOCUMENT NUMBER: 136:200471

TITLE: Preparation of D-glutamic acid derivatives as inhibitors of glutamate racemase

INVENTOR(S): De Dios, Alfonso; Ezquerra-Carrera, Jesus; McGee, James Eugene; Martin, Jose Alfredo; Prieto, Lourdes; Rubio-Esteban, Almudena; Smith, Michele Ceceil; Tebbe, Mark Joseph

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 83 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

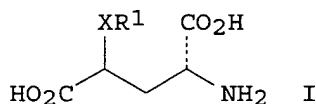
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014261	A2	20020221	WO 2001-US22589	20010809
WO 2002014261	A3	20030327		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,				

IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001078945 A5 20020225 AU 2001-78945 20010809
PRIORITY APPLN. INFO.: ES 2000-2055 A 20000810
US 2001-288361P P 20010503
WO 2001-US22589 W 20010809

OTHER SOURCE(S): MARPAT 136:200471
GI



AB Compds. I [X is a bond, O, S, SO or SO₂; R₁ = (C₁-10)alkyl, (C₂-10)alkenyl or -alkynyl, (C₄-10)alkadienyl, carboxamido- or aminocarbonyl(C₁-8)alkyl which may be substituted by (C₃-10)cycloalkyl or by one or two (un)substituted aromatic groups, provided that when X represents a bond, R₁ can not represent a 3-phenyl-2-propenyl, 3-(4-chlorophenyl)-2-propenyl, 4-fluorobenzyl or 1-naphthylmethyl group] or their esters, amides or salts were prepared as inhibitors of glutamate racemase for use as antibiotics. Thus, (2R,4S)-2-amino-4-(2-naphthyl)methylpentanedioic acid was prepared by alkylation of D-Et N-(tert-butoxycarbonyl)pyroglutamate with 2-naphthylmethyl bromide, followed by ring cleavage/deprotection using LiOH in aqueous THF and workup.

IC ICM C07C229-00

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 63

IT 1196-19-6P 9024-08-2P, Glutamate racemase 17512-59-3P 45438-73-1P
68766-96-1P 114676-59-4P 144978-35-8P **400626-15-5P**
400626-16-6P 400626-17-7P 400626-18-8P 400626-19-9P
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400626-59-7P 400626-60-0P 400626-61-1P **400626-62-2P**
400626-63-3P 400626-64-4P 400626-65-5P 400626-66-6P
400626-67-7P 400626-68-8P 400626-69-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of D-glutamic acid derivs. as inhibitors of glutamate racemase)

IT **400626-15-5P 400626-16-6P 400626-20-2P**
400626-34-8P 400626-36-0P 400626-37-1P
400626-45-1P 400626-62-2P 400626-63-3P

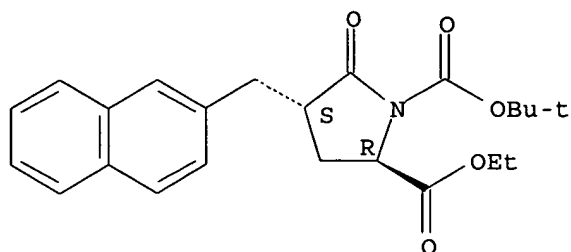
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of D-glutamic acid derivs. as inhibitors of glutamate racemase)

RN 400626-15-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenylmethyl)-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

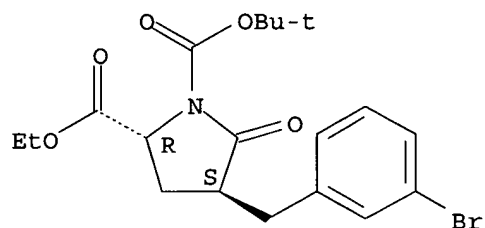
Absolute stereochemistry.



RN 400626-16-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-bromophenyl)methyl]-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

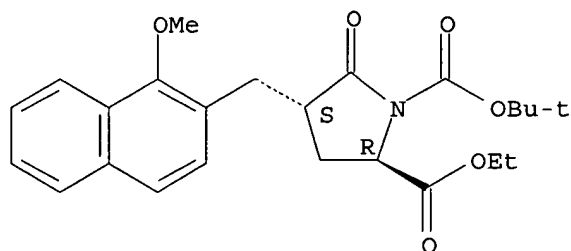
Absolute stereochemistry. Rotation (+).



RN 400626-20-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(1-methoxy-2-naphthalenyl)methyl]-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

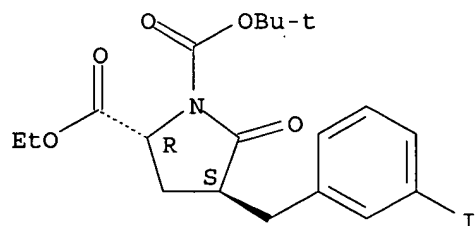
Absolute stereochemistry. Rotation (+).



RN 400626-34-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-iodophenyl)methyl]-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

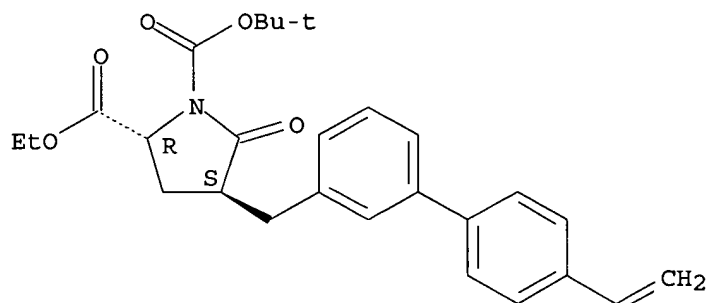
Absolute stereochemistry. Rotation (+).



RN 400626-36-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(4'-ethenyl[1,1'-biphenyl]-3-yl)methyl]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI)
(CA INDEX NAME)

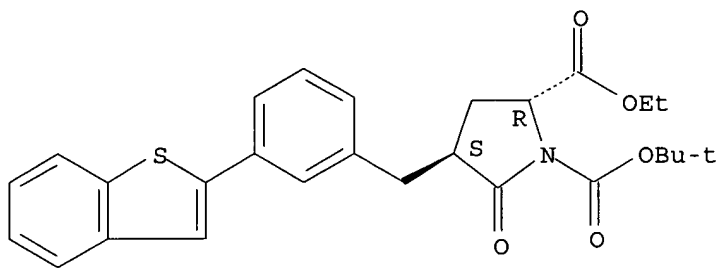
Absolute stereochemistry.



RN 400626-37-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3-benzo[b]thien-2-ylphenyl)methyl]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

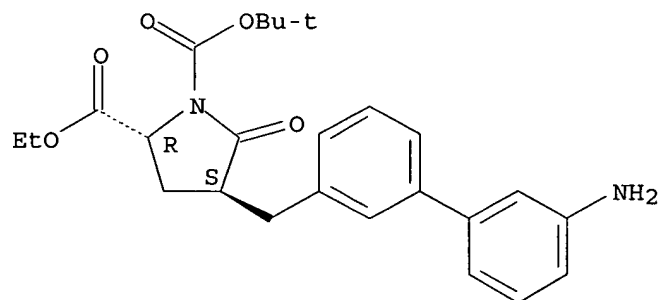
Absolute stereochemistry.



RN 400626-45-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(3'-amino[1,1'-biphenyl]-3-yl)methyl]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

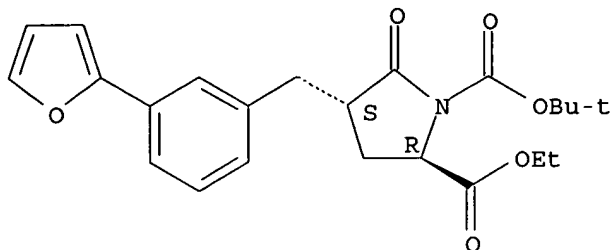
Absolute stereochemistry. Rotation (+).



RN 400626-62-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[[3-(2-furanyl)phenyl]methyl]-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

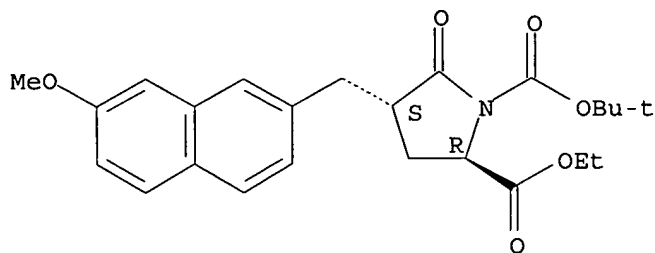
Absolute stereochemistry.



RN 400626-63-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(7-methoxy-2-naphthalenyl)methyl]-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 28 OF 61 CAPLUS COPYRIGHT 2006 ACS on STM

ACCESSION NUMBER: 2001:636072 CAPLUS

DOCUMENT NUMBER: 135:195502

TITLE: Preparation of substituted 1-phenoxy-3-pyrrolidino(or
piperidino)propan-2-ols as chemokine receptor
modulators

INVENTOR(S): Hansen, Peter; Pettersson, Lars

PATENT ASSIGNEE(S): AstraZeneca AB, Swed.

SOURCE: PCT Int. Appl., 175 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062757	A1	20010830	WO 2001-SE405	20010223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,				

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2400435	AA	20010830	CA 2001-2400435	20010223
BR 2001008678	A	20021203	BR 2001-8678	20010223
EP 1263760	A1	20021211	EP 2001-908559	20010223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003524011	T2	20030812	JP 2001-562539	20010223
PT 1263725	T	20050228	PT 2001-908558	20010223
ES 2227140	T3	20050401	ES 2001-1908558	20010223
PT 1263724	T	20050930	PT 2001-908557	20010223
ES 2241796	T3	20051101	ES 2001-1908557	20010223
ZA 2002006402	A	20031112	ZA 2002-6402	20020812
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NO 2002003932	A	20021024	NO 2002-3932	20020819
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US 6927222	B2	20050809		
PRIORITY APPLN. INFO.:			SE 2000-620	A 20000225
			SE 2000-2234	A 20000614
			SE 2000-3979	A 20001031
			WO 2001-SE405	W 20010223
OTHER SOURCE(S):			MARPAT 135:195502	
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. RCR4R5CR8(OH)CR6R7QR2 [R = I; m = 0-3; R1 = halo, CN, NO2, etc.; Q = O, S, CH2, NH; R2 = II-VII; R4-R7 = H, alkyl; or R4-R7 together = alkylene linking the two carbon atoms to which they are attached to form a 4-7 membered saturated carbocycle; or R5-R7 = H and R4 and R8 together with the carbon atoms to which they are attached form 5-6 membered saturated carbocycle; R8 = H, alkyl; R15 = CO2H, alkylcarbonyl, alkoxy carbonyl, etc.; t = 0-3; R16 = halo, CN, NO2, etc.] and their salts, useful for treating of human diseases in which modulation of chemokine receptor activity is beneficial, were prepared Thus, reacting 3-(4-chlorophenoxy)pyrrolidine (preparation given) with N-acetyl-2-(2,3-epoxypropoxy)aniline in EtOH afforded the title compound VIII.HCl. The compds. of the examples were evaluated by their ability to depress the chemotactic response to a standard concentration of MIP-1 α chemokine (no data given).

IC ICM C07D471-04

ICS C07D209-08; C07D209-26; A61K031-437; A61P011-00; A61P037-00; A61P019-00; A61P031-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT	356552-82-4P	356552-88-0P	356552-90-4P	356552-92-6P	356552-94-8P
	356552-96-0P	356552-98-2P	356553-00-9P	356553-01-0P	356553-03-2P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-ols as chemokine receptor modulators)

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-

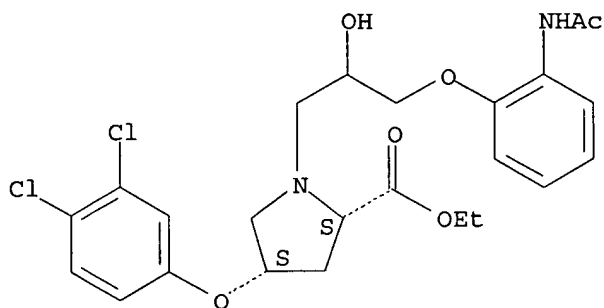
ols as chemokine receptor modulators)
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 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-ols as chemokine receptor modulators)
 RN 356557-03-4 CAPLUS
 CN L-Proline, 1-[3-[2-(acetylamino)phenoxy]-2-hydroxypropyl]-4-(3,4-dichlorophenoxy)-, ethyl ester, (4S)-, mono(trifluoroacetate) (salt) (9CI)
 (CA INDEX NAME)

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CRN 356557-02-3

CMF C24 H28 Cl2 N2 O6

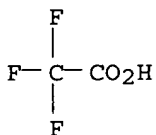
Absolute stereochemistry.



CM 2

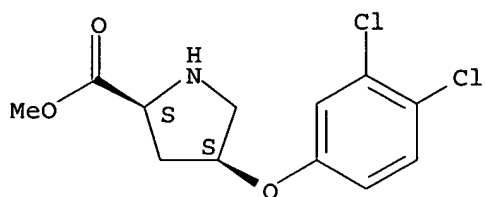
CRN 76-05-1

CMF C2 H F3 O2



IT **356558-03-7P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-ols as chemokine receptor modulators)
 RN 356558-03-7 CAPLUS
 CN L-Proline, 4-(3,4-dichlorophenoxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 29 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:636047 CAPLUS

DOCUMENT NUMBER: 135:195501

TITLE: Preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-ols as chemokine receptor modulators

INVENTOR(S): Hansen, Peter; Pettersson, Lars

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 174 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062729	A1	20010830	WO 2001-SE404	20010223
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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EP 1263725	B1	20041020		
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JP 2003523999	T2	20030812	JP 2001-561737	20010223
NZ 520719	A	20040625	NZ 2001-520719	20010223
AT 280153	E	20041115	AT 2001-908558	20010223
PT 1263725	T	20050228	PT 2001-908558	20010223
ES 2227140	T3	20050401	ES 2001-1908558	20010223
PT 1263724	T	20050930	PT 2001-908557	20010223
AU 783475	B2	20051027	AU 2001-36300	20010223
ES 2241796	T3	20051101	ES 2001-1908557	20010223
ZA 2002006402	A	20031112	ZA 2002-6402	20020812
ZA 2002006404	A	20031112	ZA 2002-6404	20020812
NO 2002003933	A	20021024	NO 2002-3933	20020819
ZA 2002006665	A	20031120	ZA 2002-6665	20020820
US 2003158225	A1	20030821	US 2002-204754	20021021
US 6951874	B2	20051004		

PRIORITY APPLN. INFO.:

SE 2000-620	A 20000225
SE 2000-2234	A 20000614
SE 2000-3979	A 20001031
WO 2001-SE404	W 20010223

OTHER SOURCE(S): MARPAT 135:195501

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. RCR4R5CR8(OH)CR6R7QR2 [I; R = II; m = 0-3; R1 = halo, CN, NO2, etc.; p = 0-1; X = O, S, CH2, etc.; Y = N, CH, C(OH) (provided that when X = O, S, CH2O, CH2NH, NH, then Y = CH); Z1 = a bond, (CH2)q (q = 1-2); Z2 = a bond, CH2 (with the proviso that Z1 and Z2 do not both simultaneously = a bond); Q = O, S, CH2, NH; R2 = III-VII; n = 0-2; R3 = alkyl, alkoxy carbonyl, CH2OH, CO2H; R4-R7 = H, alkyl; or R4-R7 together = alkylene linking the two carbon atoms to which they are attached; or R5-R7 = H and R4 and R8 together with the carbon atoms to which they are attached form 5-6 membered saturated carbocycle; R8 = H, alkyl] and their salts, useful for treating of human diseases in which modulation of chemokine receptor activity is beneficial, were prepared Thus, reacting 3-(4-chlorophenoxy)pyrrolidine (preparation given) with N-acetyl-2-(2,3-epoxypropoxy)aniline in EtOH afforded the title compound VIII. The compds. of the examples were evaluated by their ability to depress the chemotactic response to a standard concentration of MIP-1 α chemokine (no data given).

IC ICM C07D207-04

ICS C07D209-08; C07D211-06; C07D295-08; A61K031-40; A61K031-435;
A61P011-00; A61P037-00; A61P019-00; A61P031-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT	356552-82-4P	356552-88-0P	356552-90-4P	356552-92-6P	356552-94-8P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-ols as chemokine receptor modulators)

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-ols as chemokine receptor modulators)

IT **356557-03-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-ols as chemokine receptor modulators)

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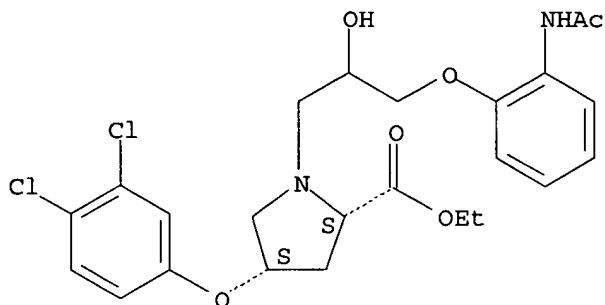
CN L-Proline, 1-[3-[2-(acetilamino)phenoxy]-2-hydroxypropyl]-4-(3,4-dichlorophenoxy)-, ethyl ester, (4S)-, mono(trifluoroacetate) (salt) (9CI)
(CA INDEX NAME)

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CRN 356557-02-3

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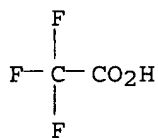
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 356558-03-7P

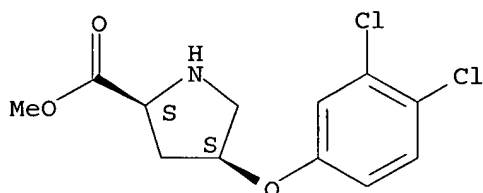
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-ols as chemokine receptor modulators)

RN 356558-03-7 CAPLUS

CN L-Proline, 4-(3,4-dichlorophenoxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 30 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:636046 CAPLUS

DOCUMENT NUMBER: 135:210941

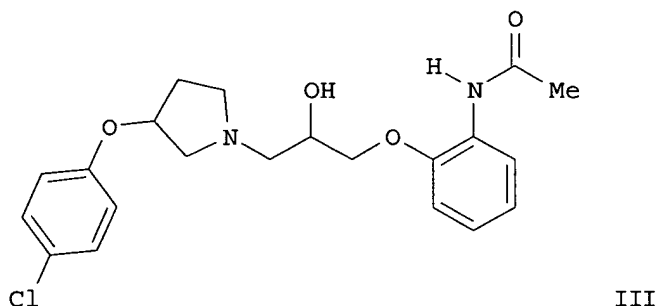
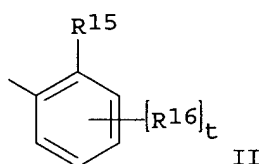
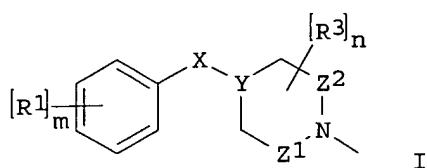
TITLE: Preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-ols as chemokine receptor modulators

INVENTOR(S): Bodkin, Michael; Eriksson, Tomas; Hansen, Peter;

Hemmerling, Martin; Henriksson, Krister; Klingstedt,
 Tomas; Pettersson, Lars
 PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
 SOURCE: PCT Int. Appl., 191 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062728	A1	20010830	WO 2001-SE403	20010223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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PRIORITY APPLN. INFO.:			SE 2000-620	A 20000225
			SE 2000-2234	A 20000614
			SE 2000-3979	A 20001031
			WO 2001-SE403	W 20010223

OTHER SOURCE(S): MARPAT 135:210941
 GI



AB The title compds. RCR4R5CR8(OH)CR6R7QR2 [R = I; m = 0-3; R1 = halo, CN, NO2, etc.; p = 0-1; X = O, S, CH2, etc.; Y = N, CH, C(OH) (provided that when X = O, S, CH2O, CH2NH, NH, then Y = CH); Z1 = a bond, (CH2)q (q = 1-2); Z2 = a bond, CH2 (with the proviso that Z1 and Z2 do not both simultaneously = a bond); Q = O, S, CH2, NH; R2 = II; n = 0-2; R3 = alkyl, alkoxy, carbonyl, CH2OH, CO2H; R4-R7 = H, alkyl; or R4-R7 together = alkylene linking the two carbon atoms to which they are attached; or R5-R7 = H and R4 and R8 together with the carbon atoms to which they are attached form 5-6 membered saturated carbocycle; R8 = H, alkyl; R15 = CO2H, alkyl, carbonyl, alkoxy, carbonyl, etc.; t = 1-3; R16 = halo, CN, NO2, etc.] and their salts, useful for treating of human diseases in which modulation of chemokine receptor activity is beneficial, were prepared. Thus, reacting 3-(4-chlorophenoxy)pyrrolidine (preparation given) with N-acetyl-2-(2,3-epoxypropoxy)aniline in EtOH afforded the title compound III.HCl. The compds. of the examples were evaluated by their ability to depress the chemotactic response to a standard concentration of MIP-1 α chemokine (no data given).

IC ICM C07D207-04

ICS C07D211-06; C07D295-08; A61K031-40; A61K031-435; A61P011-00;

A61P037-00; A61P019-00; A61P031-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-ols as chemokine receptor modulators)

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-ols as chemokine receptor modulators)

IT 356557-03-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted 1-phenoxy-3-pyrrolidino(or piperidino)propan-2-ols as chemokine receptor modulators)

RN 356557-03-4 CAPLUS

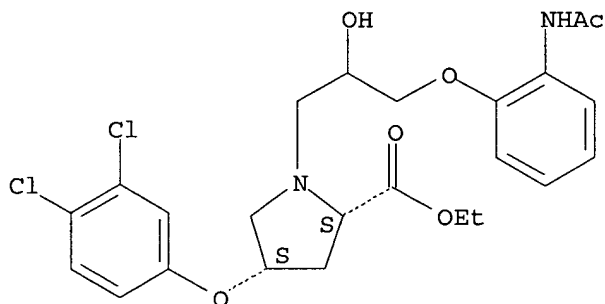
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(CA INDEX NAME)

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CRN 356557-02-3

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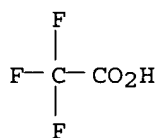
Absolute stereochemistry.



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CRN 76-05-1

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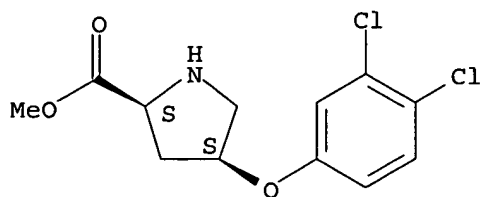
IT 356558-03-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
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RN 356558-03-7 CAPLUS

CN L-Proline, 4-(3,4-dichlorophenoxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 31 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:619582 CAPLUS

DOCUMENT NUMBER: 135:338737

TITLE: Comparative QSAR: Angiotensin II Antagonists

AUTHOR(S): Kurup, Alka; Garg, Rajni; Carini, D. J.; Hansch, Corwin

CORPORATE SOURCE: Department of Chemistry, Pomona College, Claremont, CA, 91711, USA

SOURCE: Chemical Reviews (Washington, D. C.) (2001), 101(9), 2727-2750

CODEN: CHREAY; ISSN: 0009-2665

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A QSAR study was carried out on nonpeptide angiotensin II antagonists which included a review of the literature on bioactivity and derivation of QSAR equations. The QSAR were divided into 4 groups according to the test system: rabbit, rat, guinea pig and human. Within each group, these are arranged according to potency (log I/C). Also listed is the CMR (calculated molar refractivity) which is similar to molar volume but contains a small element for polarizability, and Clog P values which give an assessment of the hydrophobic effects. The authors also used π as a measure of local hydrophobic binding sites. All the QSAR reported in the study were derived by the authors. The physicochem. parameters were autoloading from their C-QSAR databases and the QSAR regression anal. was executed with a C-QSAR program. The authors derived 39 QSAR equations which provide an overview of the structure-activity relationship for a variety of compds. To the authors knowledge, these are the first QSAR for angiotensin antagonists. The most important conclusion reached is the lack of importance of hydrophobic interactions with the receptors. The relevance of the biphenyl moiety for hydrophobicity is discussed and a model of the pharmacophore is presented.

CC 1-3 (Pharmacology)

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(comparative QSAR of nonpeptide angiotensin II antagonists)

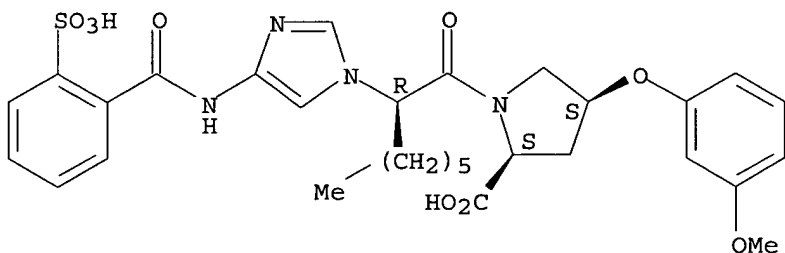
IT **164334-11-6 164334-12-7 164455-53-2**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(comparative QSAR of nonpeptide angiotensin II antagonists)

RN 164334-11-6 CAPLUS

CN L-Proline, 4-(3-methoxyphenoxy)-1-[(2R)-1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

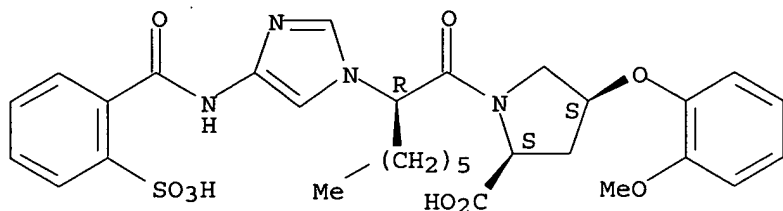


RN 164334-12-7 CAPLUS

CN L-Proline, 4-(2-methoxyphenoxy)-1-[(2R)-1-oxo-2-[4-[(2-sulfobenzoyl)amino]-

1H-imidazol-1-yl]octyl]-, (4S)- (9CI) (CA INDEX NAME)

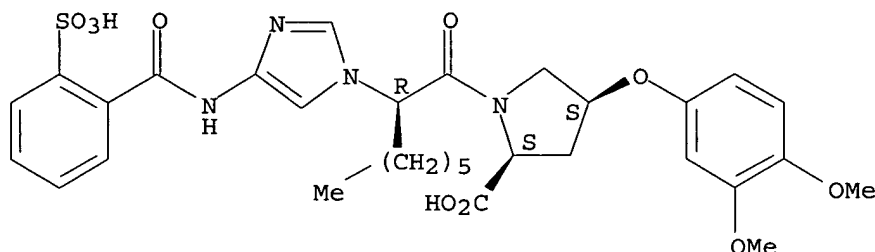
Absolute stereochemistry.



RN 164455-53-2 CAPLUS

CN L-Proline, 4-(3,4-dimethoxyphenoxy)-1-[(2R)-1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 32 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:518491 CAPLUS

DOCUMENT NUMBER: 135:318666

TITLE: A convenient and high yield method to prepare 4-hydroxypyroglutamic acids

AUTHOR(S): Zhang, X.; Schmitt, A. C.; Jiang, W.

CORPORATE SOURCE: Experimental Station, Chemical & Physical Sciences, DuPont Pharmaceuticals Company, Wilmington, DE, 19880, USA

SOURCE: Tetrahedron Letters (2001), 42(32), 5335-5338
CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:318666

AB RuO₂/NaIO₄ oxidation of N-Boc-4-silyloxy (Boc = tert-butoxycarbonyl) and 4-acetoxy proline Me esters under Et acetate/water diphase condition gave N-Boc-4-silyloxy and 4-acetoxy pyroglutamic acid derivs. in high yields. Desilylation with TBAF afforded both cis- and trans-N-Boc-methyl-4-hydroxy pyroglutamates.

CC 34-2 (Amino Acids, Peptides, and Proteins)

IT 74844-91-0P 102195-79-9P 114676-91-4P 188109-82-2P 267420-70-2P

367966-45-8P 367966-46-9P 367966-51-6P

367966-54-9P 367966-59-4P 367966-61-8P 367966-63-0P

367966-67-4P 367966-68-5P 367966-69-6P 367966-71-0P 367966-73-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation of hydroxypyroglutamic acids from hydroxyproline via catalytic oxidation and desilylation)

IT 367966-41-4P 367966-57-2P 367966-65-2P 367966-70-9P
367966-72-1P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of hydroxypyroglutamic acids from hydroxyproline via catalytic oxidation and desilylation)

IT 367966-46-9P 367966-51-6P 367966-54-9P

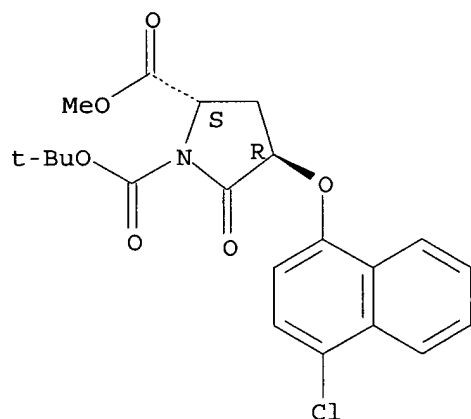
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of hydroxypyroglutamic acids from hydroxyproline via catalytic oxidation and desilylation)

RN 367966-46-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(4-chloro-1-naphthalenyl)oxy]-5-oxo-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

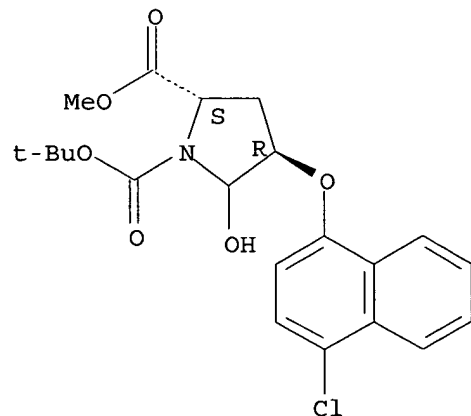
Absolute stereochemistry.



RN 367966-51-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(4-chloro-1-naphthalenyl)oxy]-5-
hydroxy-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (9CI) (CA INDEX
NAME)

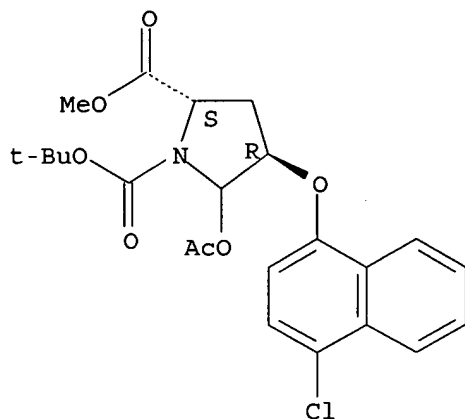
Absolute stereochemistry.



RN 367966-54-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 5-(acetyloxy)-4-[(4-chloro-1-naphthalenyl)oxy]-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



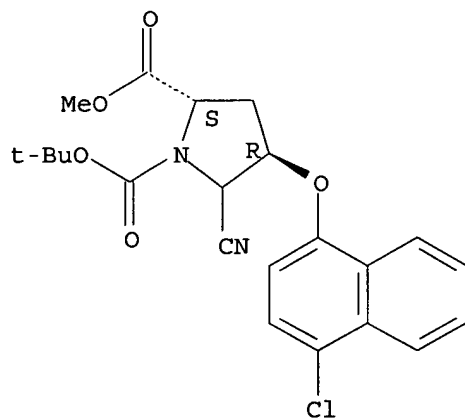
IT 367966-57-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of hydroxypyroglutamic acids from hydroxyproline via catalytic oxidation and desilylation)

RN 367966-57-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(4-chloro-1-naphthalenyl)oxy]-5-cyano-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 33 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:12266 CAPLUS

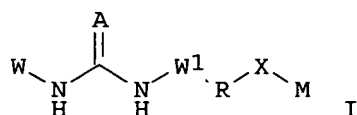
DOCUMENT NUMBER: 134:86149

TITLE: Preparation of diphenyl ureas as VLA-4 inhibitors

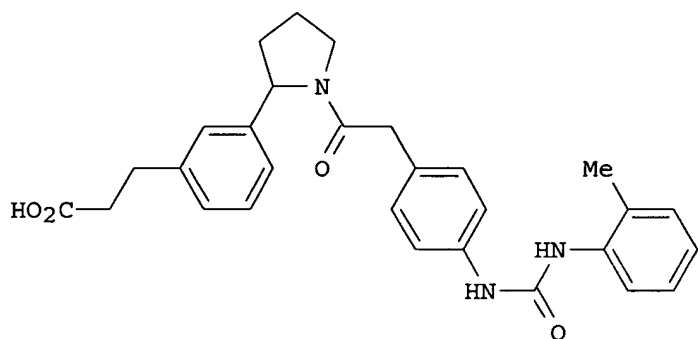
INVENTOR(S): Baldwin, John J.; McDonald, Edward; Moriarty, Kevin
Joseph; Sarko, Christopher Ronald; Machinaga, Nobuo;

PATENT ASSIGNEE(S): Nakayama, Atsushi; Chiba, Jun; Iimura, Shin; Yoneda, Yoshiyuki
 SOURCE: Daiichi Pharmaceutical Co., Ltd., Japan; Pharmacopeia, Inc.
 DOCUMENT TYPE: PCT Int. Appl., 511 pp.
 LANGUAGE: CODEN: PIXXD2
 FAMILY ACC. NUM. COUNT: Patent
 PATENT INFORMATION: English
 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000206	A1	20010104	WO 2000-US18079	20000630
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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JP 2003503350	T2	20030128	JP 2001-505915	20000630
AU 781438	B2	20050526	AU 2000-59031	20000630
RU 2264386	C2	20051120	RU 2001-135856	20000630
ZA 2001009203	A	20030207	ZA 2001-9203	20011107
NO 2001006319	A	20020228	NO 2001-6319	20011221
US 2003078249	A1	20030424	US 2001-34585	20011228
US 6756378	B2	20040629		
US 2004229858	A1	20041118	US 2004-787905	20040226
PRIORITY APPLN. INFO.:				
			US 1999-141601P	P 19990630
			US 1999-141602P	P 19990630
			US 1999-141692P	P 19990630
			WO 2000-US18079	W 20000630
			US 2001-34585	A3 20011228
OTHER SOURCE(S):				
MARPAT 134:86149				
GI				



I



II

AB The title compds. [I; W = (un)substituted aryl, heteroaryl; W1 = (un)substituted arylene, heteroarylene; A = O, S, NH; R = a bond, alkenylene, (CH₂)_n; n = 1-2; X = CO, CH₂, SO₂; M = substituted pyrrolidinyl, thiazolidinyl, etc.] which selectively inhibit the binding of ligands to α4β1 integrin (VLA-4), and therefore are useful in the treatment of conditions associated with VLA-4 mediated cell adhesion, including, but not limited to, such conditions as inflammatory and autoimmune responses, diabetes, psoriasis, inflammatory bowel disease, transplantation rejection, and tumor metastasis, were prepared E.g., a multi-step synthesis of the urea II which showed K_i of < 50 nM against VLA-4 receptors binding, was given.

IC ICM A61K031-40

ICS A61K031-4025; C07D207-12; C07D207-14; C07D401-12; C07D403-12

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT 317356-11-9P	317356-12-0P	317356-13-1P	317356-14-2P	317356-15-3P
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 317358-45-5P 317358-46-6P 317358-47-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of di-Ph ureas as VLA-4 inhibitors)

IT **317357-32-7P 317357-33-8P 317357-41-8P 317357-42-9P**

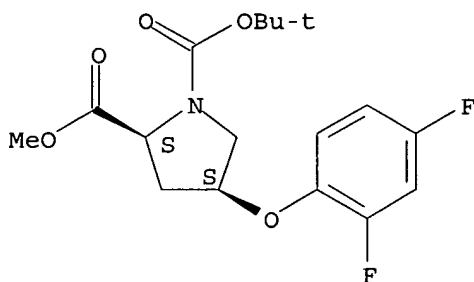
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of di-Ph ureas as VLA-4 inhibitors)

RN 317357-32-7 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2,4-difluorophenoxy)-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

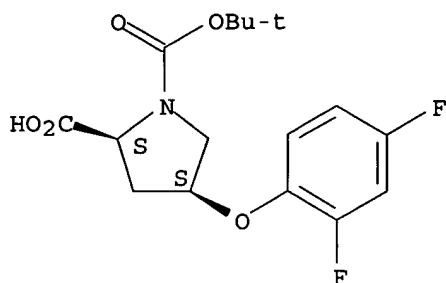
Absolute stereochemistry.



RN 317357-33-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2,4-difluorophenoxy)-, 1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

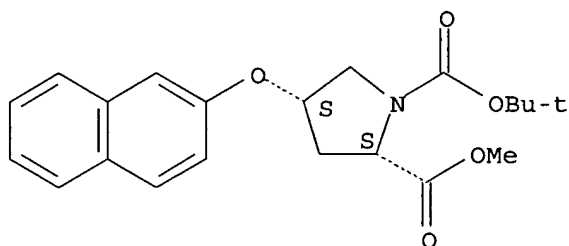
Absolute stereochemistry.



RN 317357-41-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

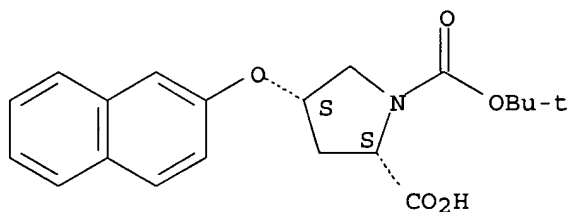
Absolute stereochemistry.



RN 317357-42-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-,
1-(1,1-dimethylethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 34 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:34889 CAPLUS

DOCUMENT NUMBER: 132:93658

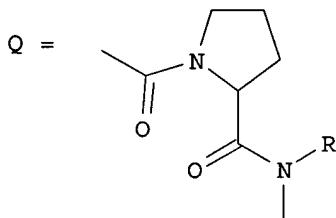
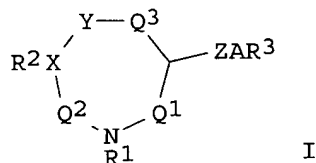
TITLE: Preparation of amino acid and peptide derivatives as
microbial efflux pump inhibitors.

INVENTOR(S): Chamberland, Suzanne; Ishida, Yohei; Lee, Ving J.;
Leger, Roger; Nakayama, Kiyoshi; Ohta, Toshiharu;
Ohtsuka, Masami; Renau, Thomas W.; Watkins, William
J.; Zhang, Zhijia J.

PATENT ASSIGNEE(S): Microcide Pharmaceuticals, Inc., USA; Daiich
Pharmaceutical Co., Ltd.

SOURCE: PCT Int. Appl., 387 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000001714	A1	20000113	WO 1999-US14871	19990629
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6399629	B1	20020604	US 1998-108906	19980701
AU 9952073	A1	20000124	AU 1999-52073	19990629
PRIORITY APPLN. INFO.:			US 1998-108906	A 19980701
			US 1998-87514P	P 19980601
			WO 1999-US14871	W 19990629
OTHER SOURCE(S):	MARPAT 132:93658			
GI				



AB A method for treating a microbial infection comprises administration of title compds. [I; Q1 = (CH₂)_{n1}; Q2 = (CH₂)_{n2}; Q3 = (CH₂)_{n3}; n1 = 0, 1; n2 = 0-3; n3 = 0-2; n1+n2+n3 = 1-4; X = N, CR2a, CR2b; R2a = H, alkyl; R2b = OH, F; Y = bond, S, O, NR23; R23 = H, alkyl; R1, R2 = H, C(:NR)R', C(:NR)NR'R'', etc.; R, R', R'' = H, alkyl; Z = bond, (CHR₄)_nCONR₄, Q, etc.; R₄ = H, alkyl, aralkyl; n = 0-3; A = bond, (CHR₅)_nX1(CHR₅)_n; X1 = O, S, bond, cycloalkylene, heterocycloalkylene; R₅ = H, alkyl; R₃ = H, (substituted) aryl, tetrahydronaphthyl, indanyl, thienyl, furyl, pyridyl, quinolyl, cycloalkyl, etc.; with provisos]. Thus, 1-(trans-4-aminomethyl-L-prolyl)-4-(3-chloro-2-methylphenyl)piperazine (solution phase preparation given)

at 2.5 µg/mL together with levofloxacin 0.25 µg/mL gave 100% inhibition of *Pseudomonas aeruginosa* PAM1001 growth.

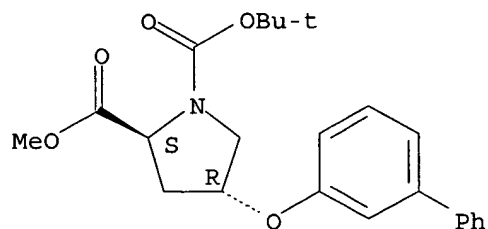
IC ICM C07K005-078

ICS A61K038-05; C07D401-12; C07D207-14; C07D207-16; C07D413-12; C07D409-12; C07D403-12; C07D403-04; C07D417-12; C07D211-60; C07K005-068

CC 34-3 (Amino Acids, Peptides, and Proteins)
 Section cross-reference(s): 1, 28

IT 2567-29-5P, 4-Phenylbenzyl bromide 2976-71-8P 27691-43-6P
29678-81-7P 33609-49-3P 36908-37-9P 40856-59-5P 40871-01-0P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of amino acid and peptide derivs. as microbial efflux pump
inhibitors)
IT 254883-51-7P 254883-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of amino acid and peptide derivs. as microbial efflux pump
inhibitors)
RN 254883-51-7 CAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 4-([1,1'-biphenyl]-3-yloxy)-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

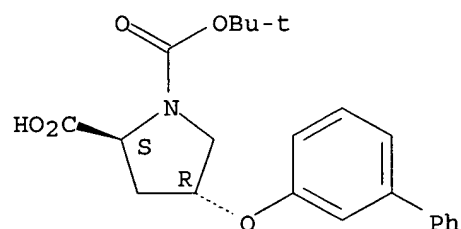
Absolute stereochemistry.



RN 254883-52-8 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-([1,1'-biphenyl]-3-yloxy)-, 1-(1,1-dimethylethyl) ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 35 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:403657 CAPLUS

DOCUMENT NUMBER: 131:165558

TITLE: The cholecystokininB receptor is coupled to two effector pathways through pertussis toxin-sensitive and -insensitive G proteins

AUTHOR(S): Pommier, Blandine; Da Nascimento, Sophie; Dumont, Stephanie; Bellier, Bruno; Million, Emmanuelle; Garbay, Christiane; Roques, Bernard P.; Noble, Florence

CORPORATE SOURCE: Departement de Pharmacochimie Moleculaire et Structurale, INSERM U266, CNRS UMR 8600, UFR des Sciences Pharmaceutiques et Biologiques, Paris, 75270, Fr.

SOURCE: Journal of Neurochemistry (1999), 73(1), 281-288
CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

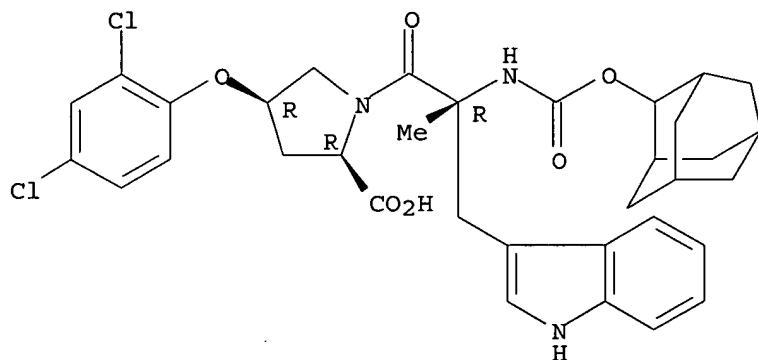
LANGUAGE: English

AB Previous binding studies have suggested the existence of two affinity states for type B cholecystokinin receptors (CCKBR), which could correspond to different coupling states of the receptor to G proteins. To test this hypothesis, we have further investigated signal transduction pathways coupled to rat CCKBR stably transfected in Chinese hamster ovary cells. We show that CCKBR are coupled to two distinct transduction pathways involving two different G proteins, a pertussis toxin-insensitive/phospholipase C pathway leading to the production of inositol phosphate and arachidonic acid, and a pertussis

toxin-sensitive/phospholipase A2 pathway leading to the release of arachidonic acid. We further demonstrate that the relative degree of activation of each effector pathway by different specific CCKBR agonists is the same, and that a specific CCKBR antagonist, RB 213, can differentially antagonize the two signal transduction pathways elicited by these agonists. Taken all together, these data could be explained by the recently proposed theory assuming that the receptor can exist in a three-state model in which two active conformations corresponding to the complex formed by the receptor with two different G proteins coexist. According to this model, agonists or antagonists could recognize preferentially either conformation of the activated receptor, leading to variable behavior in a system containing a single receptor type.

CC 2-6 (Mammalian Hormones)
 IT 25126-32-3, Cholecystokinin-8 (swine) 115295-08-4, BC 197 118101-09-0, L 365260 130930-59-5, BC 264 203563-92-2, RB 400 **211055-86-6**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (cholecystokinin B receptor coupled to two effector pathways through pertussis toxin-sensitive and -insensitive G proteins)
 IT **211055-86-6**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (cholecystokinin B receptor coupled to two effector pathways through pertussis toxin-sensitive and -insensitive G proteins)
 RN 211055-86-6 CAPLUS
 CN D-Proline, α -methyl-N-[(tricyclo[3.3.1.1^{3,7}]dec-2-yl)oxy]carbonyl]-D-tryptophyl-4-(2,4-dichlorophenoxy)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 36 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:653709 CAPLUS

DOCUMENT NUMBER: 129:276352

TITLE: Preparation of glutamic acid derivatives for the treatment of central nervous system disorders

INVENTOR(S): Pedregal Tercero, Concepcion; Rubio Esteban, Almudena

PATENT ASSIGNEE(S): LILLY S.A., Spain

SOURCE: Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

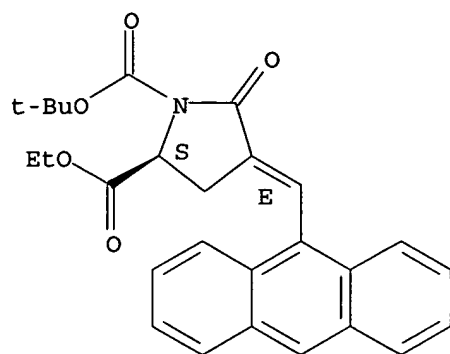
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 867430	A2	19980930	EP 1998-302168	19980324
EP 867430	A3	19981209		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
ES 2133095	A1	19990816	ES 1997-642	19970325
ES 2133095	B1	20000401		
CA 2233077	AA	19980925	CA 1998-2233077	19980324
JP 10279542	A2	19981020	JP 1998-75357	19980324
US 5990165	A	19991123	US 1998-46445	19980324
PRIORITY APPLN. INFO.:			ES 1997-642	A 19970325
OTHER SOURCE(S):	MARPAT 129:276352			
AB	Amino acid derivs. R2R3C:CR1(CH2)nCH(NH2)CO2H [n = 1, 2; R1 = CO2H, R2 = H, alkyl; R3 = H, alkyl, alkenyl, (un)substituted Ph, phenylalkyl, phenylalkenyl, diphenylalkyl, cycloalkyl, cycloalkylalkyl, or cycloalkylalkenyl or R2R3C is cycloalkyl] were prepared for the treatment of central nervous system disorders. Thus, (2S,E,E)-2-amino-4-(p-nitrocinnamylidene)pentanedioic acid was prepared by condensation of Et N-Boc-pyroglutamate with p-nitrocinnamaldehyde in the presence of lithium hexamethyldisilazide, followed by hydrolysis.			
IC	ICM C07C229-30 ICS A61K031-195			
CC	34-3 (Amino Acids, Peptides, and Proteins) Section cross-reference(s): 1			
IT	169337-98-8P 169756-84-7P 169756-85-8P 186650-01-1P 213777-86-7P 213777-87-8P 213777-88-9P 213777-89-0P 213777-90-3P 213777-91-4P 213777-92-5P 213777-93-6P 213777-94-7P 213777-95-8P 213777-96-9P 213777-97-0P 213777-98-1P 213777-99-2P 213778-00-8P 213778-01-9P 213778-02-0P 213778-03-1P 213778-04-2P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of glutamic acid derivs. for treatment of central nervous system disorders)			
IT	186650-01-1P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of glutamic acid derivs. for treatment of central nervous system disorders)			
RN	186650-01-1 CAPLUS			
CN	1,2-Pyrrolidinedicarboxylic acid, 4-(9-anthracenylmethylene)-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2S,4E)-(9CI) (CA INDEX NAME)			

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L47 ANSWER 37 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:543071 CAPLUS

DOCUMENT NUMBER: 129:161558

TITLE: Preparation and formulation of thiazolidinedione derivatives as phospholipase A2 inhibitors

INVENTOR(S): Seno, Kaoru; Ohtani, Mitsuaki; Watanabe, Fumihiko

PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan

SOURCE: PCT Int. Appl., 178 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9833797	A1	19980806	WO 1998-JP307	19980127
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
TW 577875	B	20040301	TW 1998-87101064	19980126
CA 2277947	AA	19980806	CA 1998-2277947	19980127
CA 2277947	C	20040921		
AU 9855775	A1	19980825	AU 1998-55775	19980127
AU 719210	B2	20000504		
BR 9807132	A	20000125	BR 1998-7132	19980127
EP 976748	A1	20000202	EP 1998-900741	19980127
EP 976748	B1	20031203		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
TR 9901847	T2	20000621	TR 1999-9901847	19980127
RU 2198174	C2	20030210	RU 1999-119481	19980127
AT 255579	E	20031215	AT 1998-900741	19980127
PT 976748	T	20040331	PT 1998-900741	19980127
ES 2210710	T3	20040701	ES 1998-900741	19980127
US 6147100	A	20001114	US 1999-355008	19990722
NO 9903706	A	19990930	NO 1999-3706	19990729
NO 313881	B1	20021216		

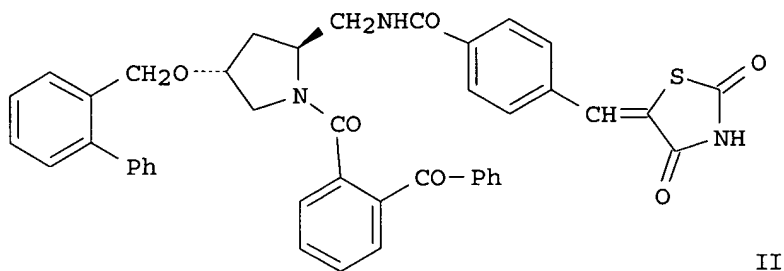
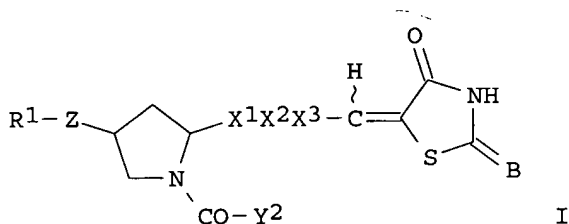
MX 9907061
PRIORITY APPLN. INFO.:

A 20000228
MARPAT 129:161558

MX 1999-7061
JP 1997-17962
WO 1998-JP307

19990729
A 19970131
W 19980127

OTHER SOURCE(S):
GI



AB The title compds., e.g. I [R1 represents optionally substituted aralkyl, etc.; Z represents optionally alkylated nitrogen, etc.; X1 represents CH2NHCO, etc.; X2 represents phenylene, etc.; X3 represents a single bond, etc.; Y2 represents optionally substituted aryl, etc.; and B represents oxygen, etc.], are prepared In an in vitro test for cPLA2 inhibition, the title compound II showed IC50 of 0.17 μ M.

IC ICM C07D417-12

ICS C07D417-14; C07D413-12; C07D455-06; A61K031-425; A61K031-42; A61K031-44; A61K031-435; A61K031-445

CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 7149-65-7P, L-Pyroglutamic acid ethyl ester 74844-91-0P 84520-67-2P
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211299-37-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of thiazolidinedione derivs. as phospholipase A2 inhibitors)

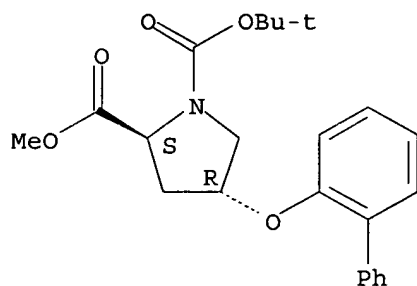
IT 211298-60-1P 211298-65-6P 211299-28-4P
211299-29-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of thiazolidinedione derivs. as phospholipase A2 inhibitors)

RN 211298-60-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-([1,1'-biphenyl]-2-yloxy)-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

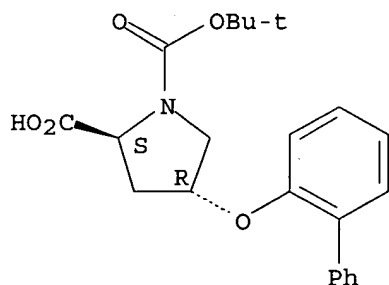
Absolute stereochemistry.



RN 211298-65-6 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-([1,1'-biphenyl]-2-yloxy)-,
1-(1,1-dimethylethyl) ester, (2S,4R)- (9CI) (CA INDEX NAME)

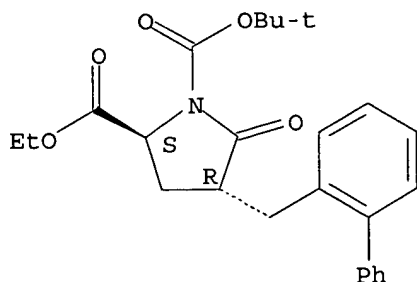
Absolute stereochemistry.



RN 211299-28-4 CAPLUS

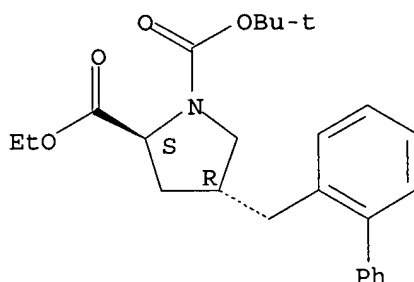
CN 1,2-Pyrrolidinedicarboxylic acid, 4-([1,1'-biphenyl]-2-ylmethyl)-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



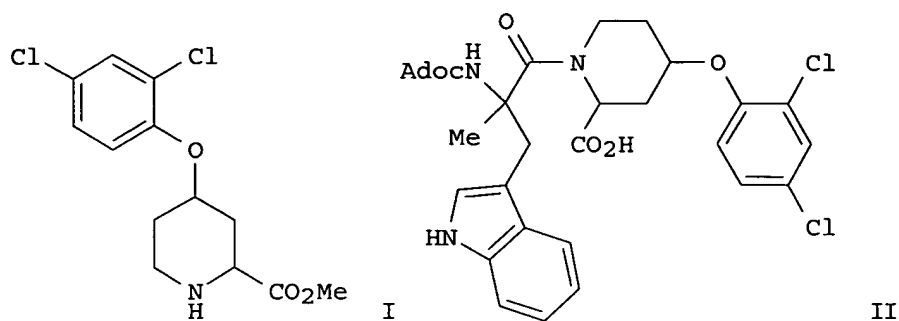
RN 211299-29-5 CAPLUS
 CN 1,2-Pyrrolidinedicarboxylic acid, 4-([1,1'-biphenyl]-2-ylmethyl)-,
 1-(1,1-dimethylethyl) 2-ethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 38 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1998:401974 CAPLUS
 DOCUMENT NUMBER: 129:175949
 TITLE: Novel constrained CCK-B dipeptoid antagonists derived from pipēcolic acid
 AUTHOR(S): Bellier, Bruno; Da Nascimento, Sophie; Meudal, Herve; Ginsel, Edith; Roques, Bernard P.; Garbay, Christiane
 CORPORATE SOURCE: Departement de Pharmacochimie Moleculaire et Structurale, INSERM U266, CNRS URA D1500 UFR des Sciences Pharmaceutiques et Biologiques, Paris, 75270, Fr.
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(11), 1419-1424
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB A new series of four 4-substituted pipecolic acid derivs. I was prepared and incorporated into dipeptoids II (Adoc = 2-adamantyloxycarbonyl). The resulting products behave as moderately potent cholecystokinin B (CCK-B) antagonists but their constrained structure and its comparison with structurally related compds. yield valuable information about the conformational requirements for optimal recognition of the CCK-B receptor by antagonists.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 2

IT **211055-86-6P**

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and structure-activity of novel constrained cholecystokinin-B dipeptoid antagonists derived from pipecolic acid)

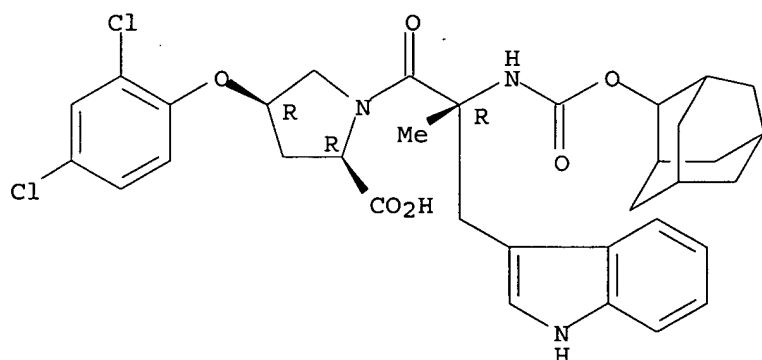
IT **211055-86-6P**

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and structure-activity of novel constrained cholecystokinin-B dipeptoid antagonists derived from pipecolic acid)

RN 211055-86-6 CAPLUS

CN D-Proline, α -methyl-N-[(tricyclo[3.3.1.1^{3,7}]dec-2-yl)oxy]carbonyl]-D-tryptophyl-4-(2,4-dichlorophenoxy)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 39 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:163563 CAPLUS
DOCUMENT NUMBER: 128:217281
TITLE: Preparation and formulation of 1-

arylsulfonylpyrrolidine-2-carboxylates as
metalloprotease inhibitors

INVENTOR(S) : Natchus, Michael George; De, Biswanath; Pikul,
Stanislaw; Almstead, Neil Gregory; Bookland, Roger
Gunnard; Taiwo, Yetunde Olabisi; Cheng, Menyan

PATENT ASSIGNEE(S) : Procter & Gamble Company, USA

SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2

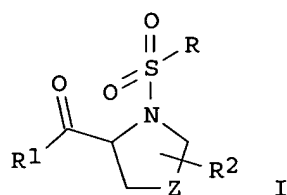
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808815	A1	19980305	WO 1997-US14555	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2263928	AA	19980305	CA 1997-2263928	19970822
AU 9740741	A1	19980319	AU 1997-40741	19970822
AU 741893	B2	20011213		
EP 927161	A1	19990707	EP 1997-938412	19970822
EP 927161	B1	20021016		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1232451	A	19991020	CN 1997-198539	19970822
BR 9713465	A	20000328	BR 1997-13465	19970822
NZ 334256	A	20001124	NZ 1997-334256	19970822
JP 2000516955	T2	20001219	JP 1998-511715	19970822
JP 3541043	B2	20040707		
AT 226193	E	20021115	AT 1997-938412	19970822
PT 927161	T	20031231	PT 1997-938412	19970822
RU 2221782	C2	20040120	RU 1999-106522	19970822
ES 2201318	T3	20040316	ES 1997-938412	19970822
IL 128666	A1	20050925	IL 1997-128666	19970822
ZA 9707698	A	19980223	ZA 1997-7698	19970827
NO 9900855	A	19990423	NO 1999-855	19990223
NO 315371	B1	20030825		
KR 2000035922	A	20000626	KR 1999-701658	19990227
HK 1020962	A1	20030808	HK 2000-100036	20000104
JP 2004115531	A2	20040415	JP 2003-384116	20031113
US 2005101567	A1	20050512	US 2004-3594	20041203
US 2005154019	A1	20050714	US 2004-3884	20041203
PRIORITY APPLN. INFO.:			US 1996-24842P	P 19960828
			JP 1998-511715	A3 19970822
			WO 1997-US14555	W 19970822
			US 1997-918317	A3 19970826
			US 2001-888675	A3 20010625
			US 2002-308780	A3 20021203
OTHER SOURCE(S) :	MARPAT 128:217281			
GI				



AB Title compds. [I; R = alkyl, (hetero)aryl, etc.; R1 = OH, alkoxy, NHOH, alkoxyamino; R2 = ≥1 of OH, alkyl, alkoxy, (hetero)aryl, etc.; Z = (CH2)1-3] were prepared as metalloprotease inhibitors (no data). Thus, cis-hydroxy-D-proline was N-acylated by 4-(MeO)C6H4SO2Cl and the esterified product amidated by N2NOK to give (2R,4S)-I [R = C6H4(OMe)-4, R1 = NHOH, R2 = H, Z = CH(OH)].

IC ICM C07D207-48

ICS A61K031-40; C07D417-04; C07D403-04; C07D401-04; C07D403-12; C07D401-12; C07D409-14; C07D413-14; C07D405-12

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 34, 63

IT 1138-54-1P 57850-07-4P 182937-63-9P 203934-42-3P 203934-63-8P
 203994-66-5P 203994-80-3P 203994-82-5P 204072-15-1P 204072-16-2P
 204072-17-3P 204072-18-4P 204072-19-5P 204072-20-8P 204072-21-9P
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 204072-27-5P **204072-28-6P** 204072-29-7P 204072-30-0P
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 204072-43-5P 204072-44-6P 204072-45-7P 204072-46-8P 204072-47-9P
 204072-49-1P 204072-50-4P 204072-51-5P 204072-52-6P 204072-53-7P
 204072-54-8P 204072-55-9P 204072-56-0P 204072-57-1P 204072-58-2P
 204072-59-3P 204072-60-6P 204072-61-7P 204072-62-8P 204072-63-9P
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 204072-99-1P 204073-00-7P 204073-01-8P 204073-02-9P 204073-03-0P
 204073-04-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and formulation of 1-arylsulfonylpyrrolidine-2-carboxylates as metalloprotease inhibitors)

IT **204072-28-6P**

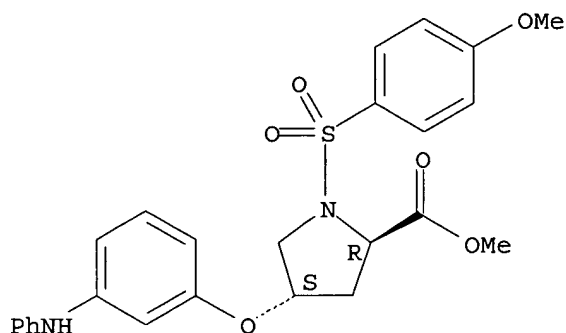
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and formulation of 1-arylsulfonylpyrrolidine-2-carboxylates as metalloprotease inhibitors)

RN 204072-28-6 CAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[3-(phenylamino)phenoxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 40 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:724028 CAPLUS

DOCUMENT NUMBER: 128:123

TITLE: Synthesis and Biological Properties of New Constrained CCK-B Antagonists: Discrimination of Two Affinity States of the CCK-B Receptor on Transfected CHO Cells

AUTHOR(S): Bellier, Bruno; McCort-Tranchepain, Isabelle; Ducos, Bertrand; Danascimento, Sophie; Meudal, Herve; Noble, Florence; Garbay, Christiane; Roques, Bernard P.

CORPORATE SOURCE: Departement de Pharmacochimie Moleculaire et Structurale, UFR des Sciences Pharmaceutiques et Biologiques, Paris, 75270, Fr.

SOURCE: Journal of Medicinal Chemistry (1997), 40(24), 3947-3956

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To improve our knowledge of the bioactive conformation of CCK-B antagonists, we have developed a new series of constrained dipeptoids whose synthesis and biochem. properties are reported here. These compds., of general structure $N\alpha$ -[(2-adamantyloxy)carbonyl]- α -methyltryptophanyl-(4-X)-proline, were designed by introducing a cyclization in the structure of the previously described CCK-B/peptoid antagonist RB 210, N-[N-[(2-adamantyloxy)carbonyl]-DL- α -methyltryptophanyl]-N-(2-phenylethyl)glycine (Blommaert et al. J. Med. Chemical 1993, 36, 2868-2877), by means of a five-membered ring. Structure-affinity relationship studies showed that an R configuration of Trp-C α and a cis configuration of the pyrrolidine substituents were favorable for receptor recognition. The most potent compds. of this new series had similar affinities for the CCK-B receptor as RB 210 and proved to be far more efficient in inhibiting inositol phosphate production in CHO cells stably transfected with rat brain CCK-B receptor, with IC50 values approaching those of the commonly used antagonists L-365,260 and PD-134,308. Moreover, binding studies performed using transfected CHO cells showed that two affinity states of the CCK-B receptor can be discriminated by some of these compds. which also have different biol. profiles and are therefore highly interesting tools for the biochem. and pharmacol. characterization of CCK-B receptor heterogeneity.

CC 1-3 (Pharmacology)

Section cross-reference(s): 13, 34

IT 198968-68-2P 198968-69-3P 198968-70-6P 198968-71-7P

198968-72-8P 198968-73-9P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(CCK-B antagonist preparation, biol. properties, and discrimination of two affinity states of CCK-B receptor on transfected CHO cells)

IT 93967-75-0P 135042-17-0P 157187-62-7P 158459-09-7P 175209-97-9P
 198968-74-0P 198968-75-1P 198968-76-2P 198968-77-3P
198968-78-4P 198968-79-5P 198968-80-8P 198968-81-9P
 198968-82-0P **198968-83-1P** **198968-84-2P** 198968-85-3P
 198968-86-4P 198968-87-5P 198968-88-6P 198968-89-7P 198968-91-1P
 198968-93-3P 198968-94-4P **198968-96-6P** 198968-98-8P
 198969-00-5P 198969-02-7P 198969-04-9P **198969-06-1P**
198969-08-3P 198969-10-7P 198969-11-8P 198969-13-0P
 198969-15-2P 198969-16-3P 198969-17-4P 198969-18-5P 198969-19-6P
198969-20-9P 198969-21-0P 198969-22-1P 198969-23-2P
 198969-24-3P 198969-25-4P 198969-26-5P 198969-27-6P 198969-28-7P
 198969-29-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction; CCK-B antagonist preparation, biol. properties,

and

discrimination of two affinity states of CCK-B receptor on transfected CHO cells)

IT **198968-68-2P**

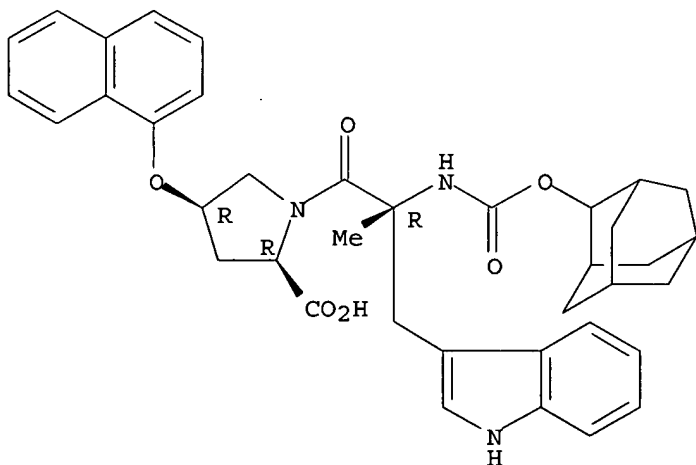
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(CCK-B antagonist preparation, biol. properties, and discrimination of two affinity states of CCK-B receptor on transfected CHO cells)

RN 198968-68-2 CAPLUS

CN D-Proline, α -methyl-N-[(tricyclo[3.3.1.1^{3,7}]dec-2-yl)oxy]carbonyl]-D-tryptophyl-4-(1-naphthalenyloxy)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **198968-78-4P** **198968-83-1P** **198968-84-2P**
198968-96-6P **198969-06-1P** **198969-08-3P**
198969-20-9P

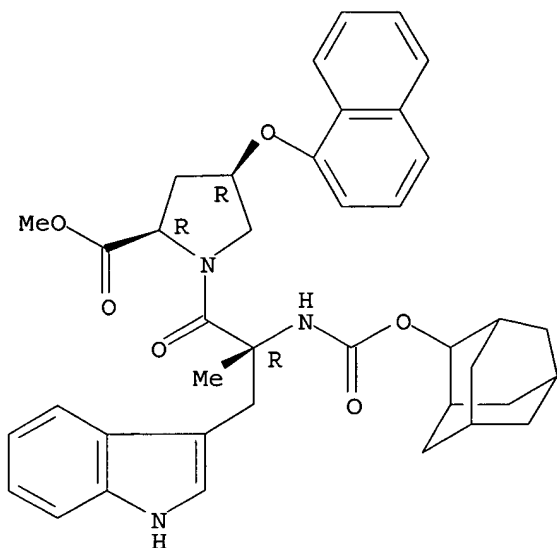
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation and reaction; CCK-B antagonist preparation, biol. properties,
and discrimination of two affinity states of CCK-B receptor on transfected
CHO cells)

RN 198968-78-4 CAPLUS

CN D-Proline, α -methyl-N-[(tricyclo[3.3.1.1^{3,7}]dec-2-yloxy)carbonyl]-D-
tryptophyl-4-(1-naphthalenyloxy)-, methyl ester, (4R)- (9CI) (CA INDEX
NAME)

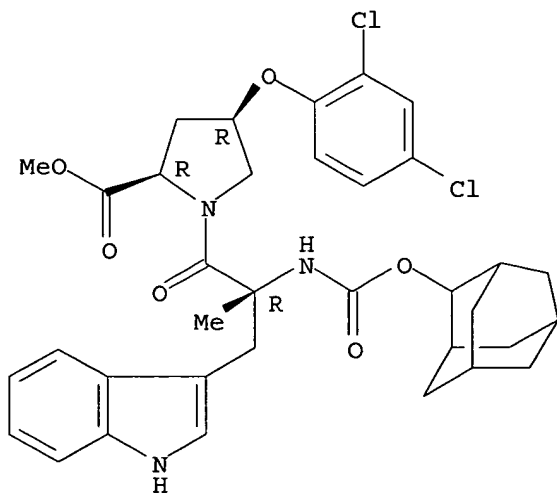
Absolute stereochemistry.



RN 198968-83-1 CAPLUS

CN D-Proline, α -methyl-N-[(tricyclo[3.3.1.1^{3,7}]dec-2-yloxy)carbonyl]-D-
tryptophyl-4-(2,4-dichlorophenoxy)-, methyl ester, (4R)- (9CI) (CA INDEX
NAME)

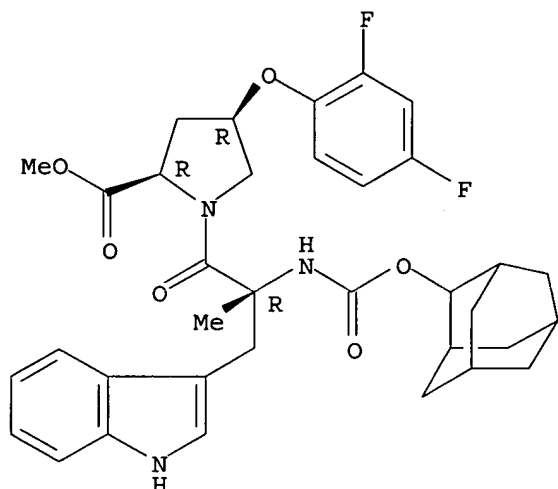
Absolute stereochemistry.



RN 198968-84-2 CAPLUS

CN D-Proline, α -methyl-N-[(tricyclo[3.3.1.1^{3,7}]dec-2-yloxy)carbonyl]-D-tryptophyl-4-(2,4-difluorophenoxy)-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 198968-96-6 CAPLUS

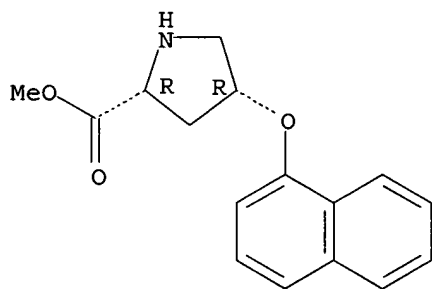
CN D-Proline, 4-(1-naphthalenyloxy)-, methyl ester, (4R)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 198968-95-5

CMF C16 H17 N O3

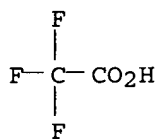
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 198969-06-1 CAPLUS

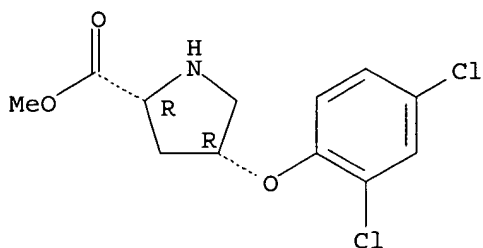
CN D-Proline, 4-(2,4-dichlorophenoxy)-, methyl ester, (4R)-, trifluoroacetate
(9CI) (CA INDEX NAME)

CM 1

CRN 198969-05-0

CMF C12 H13 Cl2 N O3

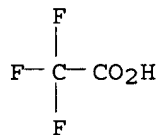
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 198969-08-3 CAPLUS

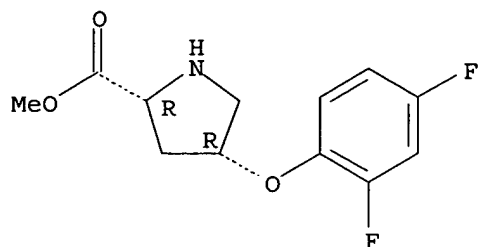
CN D-Proline, 4-(2,4-difluorophenoxy)-, methyl ester, (4R)-, trifluoroacetate
(9CI) (CA INDEX NAME)

CM 1

CRN 198969-07-2

CMF C12 H13 F2 N O3

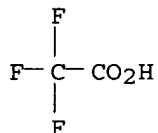
Absolute stereochemistry.



CM 2

CRN 76-05-1

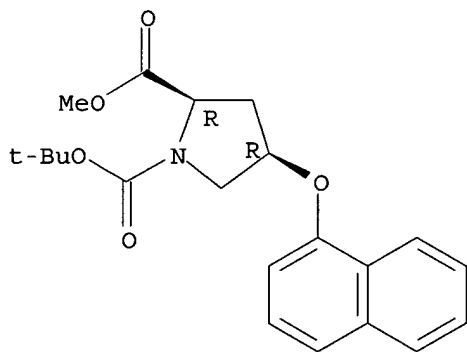
CMF C2 H F3 O2



RN 198969-20-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(1-naphthalenyloxy)-,
1-(1,1-dimethylethyl) 2-methyl ester, (2R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 41 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:39263 CAPLUS

DOCUMENT NUMBER: 126:144541

TITLE: Preparation of amino acid pharmaceuticals

INVENTOR(S): Carrera, Jesus E.; Esteban, Almudena R.; Mann, Andre;
Schoenfelder, Angele; Schoepp, Darryle D.; Tercero,
Concepcion P.; Wermuth, Camille-Georges

PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Universite Louis Pasteur;
Lilly, S.A.

SOURCE: U.S., 10 pp.

DOCUMENT TYPE: CODEN: USXXAM
 LANGUAGE: Patent
 FAMILY ACC. NUM. COUNT: English
 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5589501	A	19961231	US 1994-343817	19941122
US 5739164	A	19980414	US 1996-713624	19960913
PRIORITY APPLN. INFO.:			GB 1993-24872	A 19931203
			US 1994-343817	A3 19941122

OTHER SOURCE(S): MARPAT 126:144541

AB Amino acids R1(CH2)qCH:CH(CH2)nCHR(CH2)mCH(NH2)CO2H [R = CO2H, tetrazolyl; R1 = (un)substituted Ph, naphthyl, thienyl, etc.; m = 0-2; n, q = 0-5; p = 0, 1] and their salts and esters were prepared for use as pharmaceuticals. The amino acids possess affinity for metabotropic glutamate receptors (formulations given). Thus, (2R,4R/S)-2-amino-4-(3'-phenyl-2'-propenyl)-1,5-pentanedioic acid was prepared from (4R)-1,1-dimethylethyl 4-(3'-ethoxy-3'-oxopropenyl)-2,2-dimethyl-3-oxazolidinecarboxylate via catalytic hydrogenation, alkylation with cinnamyl bromide, oxazolidine ring cleavage by pyridinium tosylate, oxidation by pyridinium dichromate, esterification with diazomethane, and saponification

IC ICM C07C229-36
 ICS C07D257-04; A61K031-195; A61K031-41

INCL 514438000

CC 34-2 (Amino Acids, Peptides, and Proteins)
 Section cross-reference(s): 1, 63

IT **153080-94-5P** 169338-02-7P 169338-09-4P 169756-48-3P
 169756-75-6P 169756-76-7P 169756-77-8P 169756-78-9P
169756-79-0P 169756-81-4P 169756-82-5P 169756-83-6P
 169756-84-7P 169756-85-8P 169756-87-0P 169756-88-1P 169756-89-2P
 169756-92-7P 169756-93-8P 169756-94-9P **186650-01-1P**
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 186650-07-7P 186650-09-9P 186650-10-2P 186650-11-3P 186650-12-4P
 186650-13-5P 186650-14-6P 186650-15-7P 186650-16-8P 186689-18-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amino acid pharmaceuticals)

IT **153080-90-1P** 158512-77-7P 158512-78-8P 169338-20-9P
 169756-30-3P 169756-31-4P 169756-38-1P 169756-39-2P 169756-41-6P
 169756-42-7P 169756-43-8P 169756-44-9P 169756-45-0P 169756-90-5P
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 186650-18-0P 186689-11-2P 186689-14-5P 186689-16-7P 186689-21-4P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino acid pharmaceuticals)

IT **153080-94-5P 169756-79-0P 186650-01-1P**
186650-02-2P

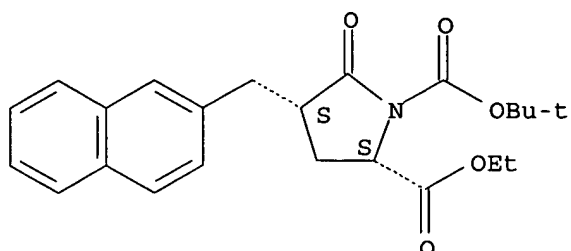
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amino acid pharmaceuticals)

RN 153080-94-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenylmethyl)-5-oxo-,
 1-(1,1-dimethylethyl) 2-ethyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

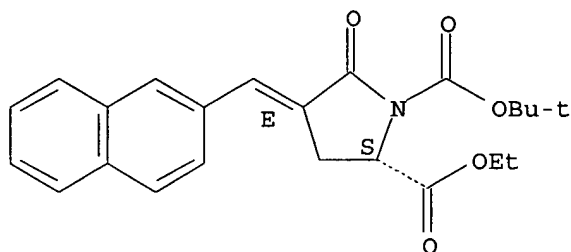
Absolute stereochemistry.



RN 169756-79-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenylmethylene)-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

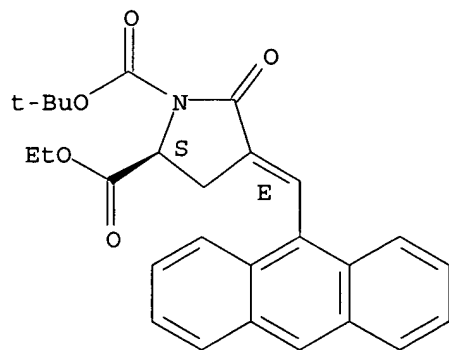
Absolute stereochemistry.
Double bond geometry as shown.



RN 186650-01-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(9-anthracenylmethylene)-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2S,4E)- (9CI) (CA INDEX NAME)

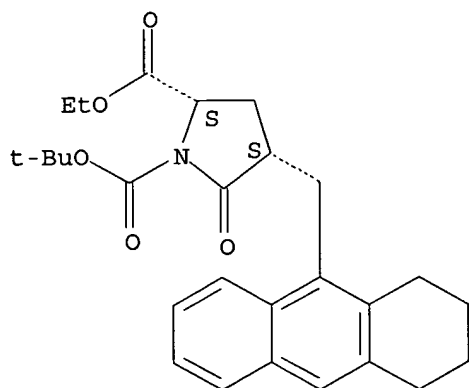
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 186650-02-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 5-oxo-4-[(1,2,3,4-tetrahydro-9-anthracenyl)methyl]-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2S-cis)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



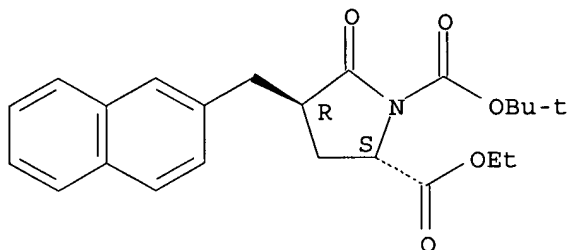
IT 153080-90-1P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid pharmaceuticals)

RN 153080-90-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenylmethyl)-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 42 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:15490 CAPLUS

DOCUMENT NUMBER: 126:60367

TITLE: Preparation of aryloxy- and arylthioglutamic acids as
excitatory amino acid receptor antagonists

INVENTOR(S): Heinz, Lawrence J.; Lunn, William H. W.; Schoepp,
Darryle D.

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: U.S., 31 pp., Cont.-in-part of U.S. Ser. No.
161,830, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5576323	A	19961119	US 1994-322632	19941013
ZA 9409405	A	19960528	ZA 1994-9405	19941128
CA 2136904	AA	19950604	CA 1994-2136904	19941129

NO 9404578	A	19950606	NO 1994-4578	19941129
AU 9479151	A1	19950608	AU 1994-79151	19941130
AU 676781	B2	19970320		
BR 9404809	A	19950801	BR 1994-4809	19941201
FI 9405704	A	19950604	FI 1994-5704	19941202
EP 658539	A1	19950621	EP 1994-308949	19941202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 69181	A2	19950828	HU 1994-3469	19941202
CN 1108240	A	19950913	CN 1994-119360	19941202
JP 07267908	A2	19951017	JP 1994-299390	19941202
US 5843997	A	19981201	US 1996-626447	19960402
PRIORITY APPLN. INFO.:			US 1993-161830	B2 19931203
			US 1994-322632	A 19941013

OTHER SOURCE(S): MARPAT 126:60367

AB Novel compds. R₃pX₃mX₂sX₁nCH(CO₂R₂)(CH₂)_rCH(NH₂)CO₂R₁ [R₁, R₂ = H, protective group, R₃, X₂ = (un)substituted aryl or heterocycllyl group, X₁ = NH₂ or substituted amino, O, S, X₃ = alkylene, alkenediyl, oxoalkylene, oxyalkylene, etc., m, n, s = 0, 1, p = 0-3, q = 0-6, r = 1, 2] or their pharmaceutically acceptable salts were prepared as antagonists of excitatory amino acid receptors. Thus, Me 3-hydroxy-2-pyrrolidone-5-carboxylate was prepared in 4 steps from cyclopentadiene and benzyl N-hydroxycarbamate and etherified with phenol and treated with LiOH in H₂O-THF to afford 4-phenoxyglutamic acid. The latter at 10 µM concentration gave 88.0% displacement of 3H-glutamate binding from rat brain cell membranes. Formulation containing the title compds. are given.

IC ICM A61K031-435

ICS A61K031-41; A61K031-34; A61K031-195

INCL 514277000

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 63

IT 1081-75-0P, 1,3-Diphenylpropane 1083-56-3P, 1,4-Diphenylbutane
 1087-49-6P, 1,6-Diphenylhexane 34591-21-4P 36940-99-5P 99027-88-0P
 110590-27-7P 113138-08-2P 113795-46-3P 170012-55-2P 170012-56-3P
 170012-58-5P 170012-59-6P 170012-60-9P 170012-66-5P 170012-67-6P
 170012-68-7P 170012-69-8P 170012-70-1P 170012-71-2P 170012-72-3P
 170012-73-4P 170012-76-7P 170012-77-8P 185320-06-3P
 185320-08-5P 185320-13-2P 185320-15-4P
 185320-16-5P 185320-17-6P 185320-33-6P 185320-34-7P
 185320-37-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of aryloxy- and arylthioglutamic acids as excitatory amino acid receptor antagonists)

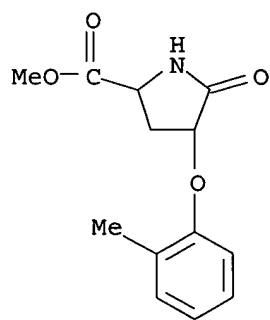
IT 185320-08-5P 185320-15-4P 185320-16-5P
 185320-17-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

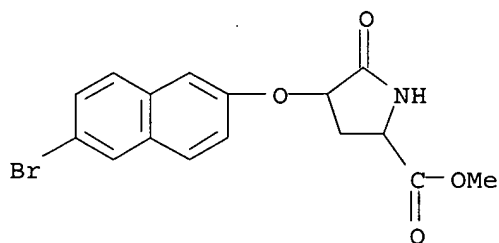
(preparation of aryloxy- and arylthioglutamic acids as excitatory amino acid receptor antagonists)

RN 185320-08-5 CAPLUS

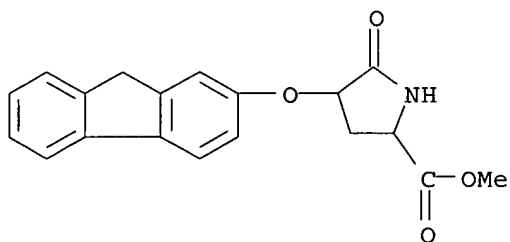
CN Proline, 4-(2-methylphenoxy)-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



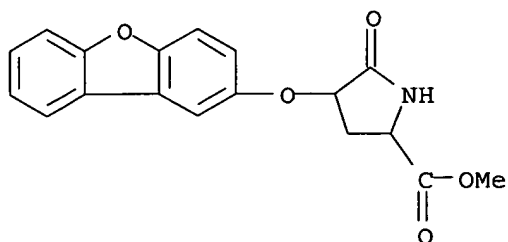
RN 185320-15-4 CAPLUS
 CN Proline, 4-[(6-bromo-2-naphthalenyl)oxy]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



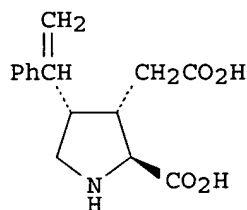
RN 185320-16-5 CAPLUS
 CN Proline, 4-(9H-fluoren-2-yloxy)-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 185320-17-6 CAPLUS
 CN Proline, 4-(2-dibenzofuranyloxy)-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



L47 ANSWER 43 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1996:513743 CAPLUS
 DOCUMENT NUMBER: 125:157768
 TITLE: Synthesis of a Series of Aryl Kainic Acid Analogs and Evaluation in Cells Stably Expressing the Kainate Receptor humGluR6
 AUTHOR(S): Cantrell, Buddy E.; Zimmerman, Dennis M.; Monn, James A.; Kamboj, Rajender K.; Hoo, Ken H.; Tizzano, Joseph P.; Pullar, Ian A.; Farrell, Louise N.; Bleakman, David
 CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA
 SOURCE: Journal of Medicinal Chemistry (1996), 39(19), 3617-3624
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



I

AB The synthesis and pharmacol. characterization of a novel series of 4-aryl-substituted kainic acid analogs are described. Receptor affinities were determined on recombinantly expressed humGluR6 kainate receptors and on [3H]kainate binding to rat forebrain kainate receptors. Functional agonist potencies were assessed using whole cell voltage clamp recordings in cells expressing humGluR6 receptors. Substitution of Ph for the Me at the C-4 position of kainic acid produced I which has high affinity and agonist potency at the GluR6 receptor. Substitution on Ph led to a series of compds. with varying affinity for this kainate receptor. Agonist potency correlated with receptor affinity and with no derivative could antagonist activity be identified. Affinities for the humGluR6 kainate receptor were approx. 10-50 less than the observed affinities at rat forebrain kainate receptors. However, within the series of 4-aryl-substituted kainic acid analogs, there was a high degree of correlation between the functional potency and binding affinities for

humGluR6 receptors and competition with kainate binding to rat forebrain kainate receptors.

CC 1-3 (Pharmacology)

Section cross-reference(s): 26

IT 180208-02-0P 180208-03-1P 180208-04-2P 180208-05-3P 180208-06-4P
180208-07-5P 180208-08-6P 180208-09-7P 180208-10-0P 180208-11-1P
180208-12-2P 180208-13-3P 180208-14-4P 180208-15-5P 180208-16-6P
180208-17-7P 180208-18-8P 180208-19-9P 180208-20-2P 180208-21-3P
180208-22-4P 180208-23-5P 180208-24-6P 180208-25-7P 180208-26-8P
180208-27-9P 180208-28-0P 180208-29-1P 180208-30-4P
180208-31-5P 180324-06-5P 180324-07-6P 180324-08-7P
180324-09-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of aryl kainic acid analogs and evaluation in cells stably expressing the kainate receptor humGluR6)

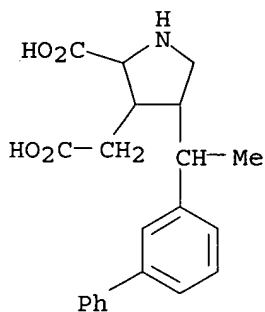
IT **180208-31-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of aryl kainic acid analogs and evaluation in cells stably expressing the kainate receptor humGluR6)

RN 180208-31-5 CAPLUS

CN 3-Pyrrolidineacetic acid/ 4-(1-[1,1'-biphenyl]-3-ylethyl)-2-carboxy- (9CI)
(CA INDEX NAME)



L47 ANSWER 44 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:994458 CAPLUS

DOCUMENT NUMBER: 124:87807

TITLE: Preparation of argininealdehyde containing peptides as antithrombotic agents.

INVENTOR(S): Kurz, Kenneth Dean; Rothenberger, Robert Berkey; Sall, Daniel Jon; Shuman, Robert Theodore; Smith, Gerald Floyd; Wiley, Michael Robert

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: Eur. Pat. Appl., 38 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

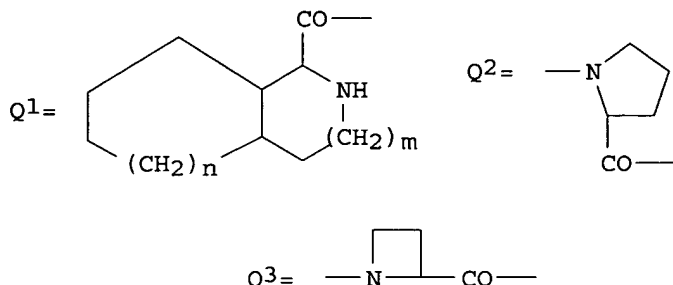
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 672665 A1 19950920 EP 1995-301388 19950303
 EP 672665 B1 20010207
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
 CA 2143533 AA 19950905 CA 1995-2143533 19950228
 US 5578574 A 19961126 US 1995-397452 19950302
 JP 07278092 A2 19951024 JP 1995-43916 19950303
 ES 2153875 T3 20010316 ES 1995-301388 19950303
 PRIORITY APPLN. INFO.: US 1994-206554 A 19940304
 OTHER SOURCE(S): MARPAT 124:87807
 GI



AB XYNHCH(CHO)(CH₂)₃NHC(:NH)NH₂ [X = (substituted) homoprolinyl, prolinyl, (iso)thiazolidinoyl, (thio)morpholinoyl, piperazinoyl, (is)oxazolidinoyl, 2-azanorbornoyl, Q¹, etc.; Y = Q², Q³; n = 1-3; m = 2, 3], were prepared. Thus, D-homoprolinylprolinylargininealdehyde dihydrochloride (D-hPro-Pro-Arg-H.2HCl), prepared by solution phase methods via coupling of Z-hPro-Pro-OH (preparation given) with Arg(Z) lactam hydrochloride (preparation given) in a canine model of coronary artery thrombosis at 1.0 mg/kg/h showed a time to occlusion of >225 min.

IC ICM C07D401-06

ICS A61K031-445; C07D403-06; A61K031-40; C07D417-06

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT 13206-31-0P 28697-09-8P 51219-18-2P 51219-20-6P 72744-87-7P
 81344-50-5P 111944-09-3P 155075-23-3P 171180-97-5P 171180-98-6P
171181-00-3P 171181-09-2P 171181-10-5P 171181-11-6P
 171181-12-7P 171181-13-8P 171181-14-9P 171181-15-0P 171181-17-2P
 171335-94-7P 171335-95-8P 171335-96-9P 172494-40-5P 172494-41-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of argininealdehyde containing peptides as antithrombotic agents)

IT **171181-00-3P**

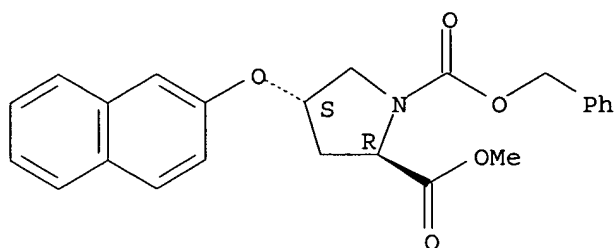
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of argininealdehyde containing peptides as antithrombotic agents)

RN 171181-00-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-, 2-methyl 1-(phenylmethyl) ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 45 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:969443 CAPLUS

DOCUMENT NUMBER: 124:30433

TITLE: Preparation of bisulfite adducts of arginine aldehyde derivatives or arginine aldehyde-containing peptides as thrombin inhibitors and anticoagulants.

INVENTOR(S): Ruterbories, Kenneth James; Shuman, Robert Theodore

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: Eur. Pat. Appl., 122 pp.

CODEN: EPXXDW

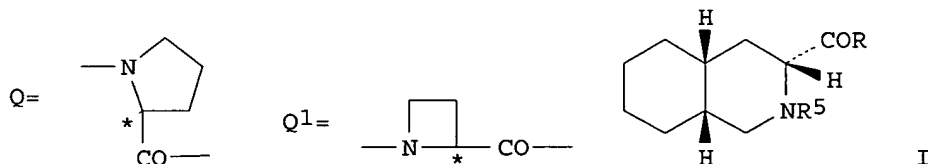
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 670310	A1	19950906	EP 1995-301389	19950303
EP 670310	B1	19980902		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2143532	AA	19950905	CA 1995-2143532	19950228
JP 07278095	A2	19951024	JP 1995-43919	19950303
AT 170508	E	19980915	AT 1995-301389	19950303
ES 2120132	T3	19981016	ES 1995-301389	19950303
PRIORITY APPLN. INFO.:			US 1994-206579	A 19940304
OTHER SOURCE(S):	MARPAT 124:30433			
GI				



AB X-Y-NHCH[(CH₂)₃NHC(:NH)NH₂]C(OH)SO₃-M+ [X = (un)substituted homoprolinyl, prolinyl, thiazolidinoyl, isothiazolidinoyl, thiomorpholinoyl, piperazinoyl, morpholinoyl, oxazolidinoyl, isoxazolidinoyl, 2-azanorbornoyl, R₃C(Z)(Z₁R₄)CO, R₈NHCHR₇CHR₆CO, etc.; wherein Z = H, HO, C₁-4 alkoxy, (un)substituted NH₂; R₃ = H, C₁-4 alkyl, (un)substituted Ph or CH₂Ph; Z₁ = a bond, CH₂; R₄ = C₁-6 alkyl, C₁-4 alkoxy, cyclopentyl, cyclohexyl, (un)substituted (hetero)aryl; when Z = (un)substituted NH₂, it can be taken together with R₃ to form an azetidiny, a 5- or 6-membered (un)substituted saturated N-containing heterocyclic ring, or a 9- or 10-membered

(un)substituted fused bicyclic N-containing heterocyclic group; or R3 and R4 can be taken together to form a cyclopentyl, cyclohexyl, or a 9- or 10-membered (un)substituted bicyclic hydrocarbyl; R6, R7 = H, C1-4 alkyl, (un)substituted Ph, cyclopentyl, cyclohexyl, etc.; R8 = H, C1-4 alkyl, C1-4 alkyl-S(O)q; wherein q = 0-2; Y = Q, Q1; M = a pharmaceutically acceptable alkali or alkaline earth metal] are prepared These bisulfite

adducts

can inhibit the epimerization and maintain the L-configuration for the arginine residue. Thus, D-phenylalanine was refluxed with a mixture of 37% formaldehyde and concentrated HCl for 3.4 h to give 45% D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid which was hydrogenated in the presence of 5% Rh/Al2O3 at 2,000 psi H pressure in a mixture of H2O and concentrated HCl to

give

100% D-cis-(4aS,8aS)-perhydro-3-isoquinolinecarboxylic acid (I; R = OH, R5 = H). This compound was acylated by benzyl chloroformate in aqueous THF with maintaining the pH of the solution at 10.0 by adding 2 N aqueous NaOH to give

85%

I (R = OH, R5 = PhCH2O2C) which was condensed with H-Pro-OCMe3 using DCC and 1-hydroxybenzotriazole in DMF at 0° for 3 h and room temperature for 24 h to give 94% I (R = Pro-OCMe3, R5 = PhCH2O2C). The latter compound was deprotected with CF3CO2H in anisole to give, after workup, 49% I (R = Pro-OH, R5 = PhCH2O2C) which was treated with iso-Bu chloroformate in the presence of n-methylmorpholine in DMF at -15° and condensed with HCl.H-Arg(Z)-lactam in the presence of diisopropylethylamine at -15° for 4 h to give I [R = Pro-Arg(Z)-lactam, R5 = PhCH2O2C]. This lactam was reduced by LiAlH4 in THF at -65° for 30 min to give, after workup, a protected arginal derivative I [R = Pro-Arg(Z)-H, R5 = PhCH2O2C] which was hydrogenated in the presence of 5% Pd-C in a mixture of EtOH, H2O, and H2SO4 for 3 h to give an arginal derivative I.H2SO4 (R = Pro-Arg-H, R5 = H). The latter compound was dissolved in H2O and treated with NaHSO3 to give, after lyophilization, 100% I .H2SO4 [R = Pro-NHCH[(CH2)3NHC(:NH)NH2]CH(OH)SO3Na, R5 = H]. This compound inhibited human thrombin, trypsin, plasmin, and tissue-type plasminogen activator (t-PA) with k value of 62, 137, 2.7, and 0.01, resp., and showed the index of bioavailability of 57% in rats.

IC

ICM C07D207-16

ICS A61K031-40; C07K005-06; C07D401-06

CC

34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 7

IT

565-07-1P 2133-34-8P 3381-60-0P 5211-23-4P 6742-26-3P
 13206-31-0P 14440-98-3P 19832-04-3P, 2-Piperidinylacetic acid
 26011-68-7P 28697-09-8P 29738-09-8P 51219-18-2P 51219-20-6P
 64471-88-1P 69812-46-0P 72744-87-7P 78190-11-1P,
 N-Benzoyloxycarbonylnipecotic acid 81344-50-5P 91564-21-5P,
 3-Amino-2-benzylpropionic acid 100481-09-2P, 2-Thiazolesulfonyl chloride
 103733-65-9P 103831-16-9P 103831-17-0P 108645-16-5P 110599-67-2P
 111944-09-3P 129042-71-3P 130930-25-5P 131472-74-7P, Methyl
 N-diphenylmethyle-L-phenylalaninate 132616-93-4P 137428-09-2P
 138774-74-0P 144644-00-8P 155075-23-3P 160732-86-5P 164150-62-3P
 164150-63-4P 164150-64-5P 164150-66-7P 164150-67-8P 164150-68-9P
 169390-25-4P 169820-87-5P 169820-88-6P 170846-05-6P,
 N-Benzoyloxycarbonyl-N-methyl-3-amino-2-benzylpropionic acid 171180-97-5P
 171180-98-6P 171180-99-7P 171181-00-3P 171181-01-4P
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 171181-98-9P 171182-01-7P 171182-02-8P 171182-03-9P,
 N-Benzyloxycarbonyl-N-methyl-DL-3-amino-3-phenylpropionic acid
 171182-04-0P, N-Benzyloxycarbonyl-3-amino-3-cyclohexylpropionic acid
 171182-05-1P, N-Benzyloxycarbonyl-N-methyl-3-amino-3-cyclohexylpropionic
 acid 171182-06-2P, Ethyl N-benzyloxycarbonyl-3-amino-2-benzylpropionate
 171182-07-3P, N-Benzyloxycarbonyl-3-amino-2-benzylpropionic acid
 171182-08-4P 171182-09-5P 171335-94-7P 171335-95-8P 171335-96-9P
 171335-97-0P 171335-98-1P 171335-99-2P 171336-00-8P 171336-01-9P
 171336-02-0P 171336-03-1P 171336-06-4P 171336-07-5P 171336-08-6P
 171482-03-4P 171594-47-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of bisulfite adducts of arginine aldehyde derivs. or arginine aldehyde-containing peptides as thrombin inhibitors and anticoagulants.)

IT 171181-00-3P

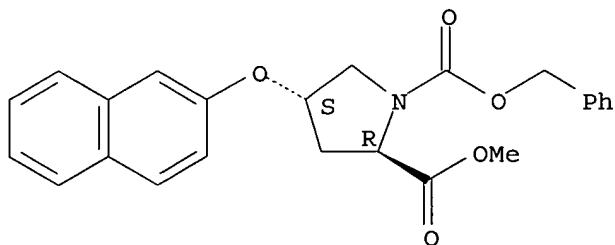
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of bisulfite adducts of arginine aldehyde derivs. or arginine aldehyde-containing peptides as thrombin inhibitors and anticoagulants.)

RN 171181-00-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-, 2-methyl 1-(phenylmethyl) ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 46 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:905329 CAPLUS

DOCUMENT NUMBER: 123:314527

TITLE: Preparation of aryloxyglutamates and related compounds as excitatory amino acid receptor antagonists.

INVENTOR(S): Heinz, Lawrence J.; Lunn, William Henry Walker; Schoepp, Darryle Darwin

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: Eur. Pat. Appl., 52 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 658539	A1	19950621	EP 1994-308949	19941202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5576323	A	19961119	US 1994-322632	19941013
PRIORITY APPLN. INFO.:			US 1993-161830	A 19931203
			US 1994-322632	A 19941013

OTHER SOURCE(S): CASREACT 123:314527; MARPAT 123:314527

AB H2NCH(CO2R3)(CH2)rCH(CO2R4)Zn(R1)sWm(R2)p [Z = NR5, O, S; W = CH3-p, (CH2)q, CH:CHCO, (CH2)qO, NR5, O, S, SO, SO2, etc.; m, n, s = 0, 1; p = 0-3; q = 0-6; r = 1, 2; m + n + p + s ≥ 1; R1, R2 = (substituted) aryl, heterocyclyl; R3, R4 = H, protecting group; R5 = H, alkyl, acyl, alkylsulfonyl; with provisos], were prepared Thus, Me 3-hydroxy-2-pyrrolidone-5-carboxylate (preparation given) was treated with Ph3P, 2-naphthalenethiol, and di-Et azodicarboxylate in THF at 0° to give Me 3-(2-naphthalenethio)-2-pyrrolidone-5-carboxylate. The latter was treated with LiOH in THF/H2O to give 3-(2-naphthalenethio)glutamic acid. This at 100 μM gave 100.6% displacement of [3H]-Glu from crude rat forebrain membrane preps.

IC ICM C07C229-24

ICS C07D257-04; C07D307-91; C07D249-10; C07D207-28; A61K031-195

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 63

IT 1081-75-0P 1083-56-3P 1087-49-6P 34591-21-4P 36940-99-5P
 99027-88-0P 110590-27-7P 113138-08-2P 113795-46-3P 170012-55-2P
 170012-56-3P 170012-58-5P 170012-59-6P 170012-60-9P 170012-65-4P
 170012-66-5P 170012-67-6P 170012-68-7P 170012-69-8P 170012-70-1P
 170012-71-2P 170012-72-3P 170012-73-4P 170012-76-7P 170012-77-8P
 170012-78-9P 185320-06-3P 185320-08-5P 185320-13-2P
 185320-15-4P 185320-16-5P 185320-17-6P
 185320-33-6P 185320-34-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of aryloxyglutamates and related compds. as excitatory amino acid receptor antagonists)

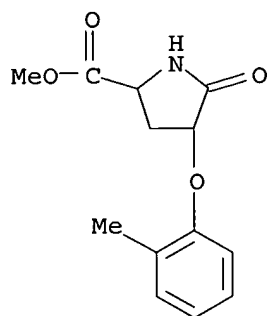
IT 185320-08-5P 185320-15-4P 185320-16-5P
 185320-17-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

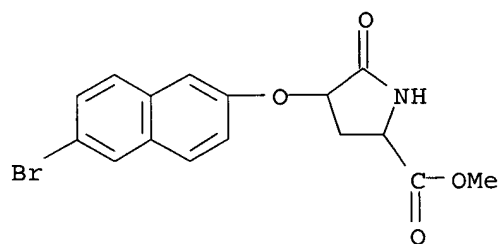
(preparation of aryloxyglutamates and related compds. as excitatory amino acid receptor antagonists)

RN 185320-08-5 CAPLUS

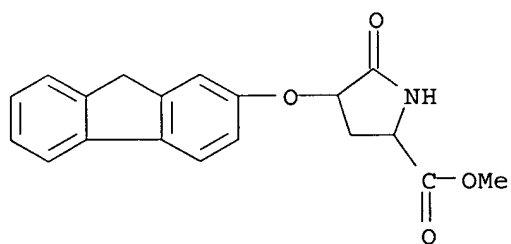
CN Proline, 4-(2-methylphenoxy)-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



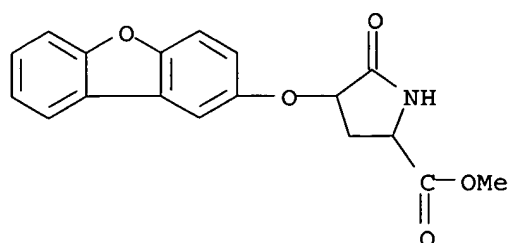
RN 185320-15-4 CAPLUS
 CN Proline, 4-[(6-bromo-2-naphthalenyl)oxy]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 185320-16-5 CAPLUS
 CN Proline, 4-(9H-fluoren-2-yloxy)-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 185320-17-6 CAPLUS
 CN Proline, 4-(2-dibenzofuranyloxy)-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



L47 ANSWER 47 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:899178 CAPLUS

DOCUMENT NUMBER: 123:306600

TITLE: Antithrombotic L-arginine aldehyde derivatives

INVENTOR(S): Chirgadze, Nickolay Yuri; Schacht, Aaron Leigh; Smith, Gerald Floyd; Willey, Michael Robert

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: PCT Int. Appl., 129 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9523608	A1	19950908	WO 1995-US2552	19950303
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9501618	A	19960827	ZA 1995-1618	19950227
US 5599793	A	19970204	US 1995-397449	19950302
CA 2180141	AA	19950908	CA 1995-2180141	19950303
AU 9519751	A1	19950918	AU 1995-19751	19950303
EP 749316	A1	19961227	EP 1995-912668	19950303
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09509936	T2	19971007	JP 1995-523001	19950303
TW 400327	B	20000801	TW 1995-84102065	19950304
PRIORITY APPLN. INFO.:			US 1994-207491	A 19940304
			WO 1995-US2552	W 19950303

OTHER SOURCE(S): CASREACT 123:306600; MARPAT 123:306600

AB L-arginine aldehyde derivs. XYNHCH(CHO)(CH₂)₃NHC(:NH)NH₂ [X = prolyl, homoprolyl, substituted cycloalkylalkanoyl, (substituted) isoquinolinecarbonyl, etc.; Y = substituted prolyl] are prepared for use as thrombin inhibitors, coagulation inhibitors, and thromboembolic disorder agents. Thus, the plasma thrombin time in rats was doubled by D-homoprolyl-L-cis-4-methylprolyl-L-argininal-2HCl (I) at 60 ng/mL. I was prepared by stepwise condensation of Cbz-D-homoproline, 4-cis-methylproline Et ester (prepared from Cbz-4-trans-Hyp Et ester), and Arg(Cbz) lactam-2HCl [prepared from Boc-Arg(Cbz)], reduction with LiAl(OCMe₃)₃, and hydrogenolysis over Pd/C.

IC ICM A61K038-00

ICS C07K005-00; C07K007-00; C07K017-00; C07D223-16; C07D251-00;

C07D251-40; C07D239-00; C07D237-00; C07D471-00; C07D487-00;
 C07D417-00; C07D285-00; C07D513-00; C07D285-08; C07D285-14;
 C07D277-04; C07D277-18; C07D277-38; C07D275-02

CC 1-8 (Pharmacology)

Section cross-reference(s): 34

IT 28697-09-8P 33996-30-4P 51219-18-2P 51219-20-6P 77513-40-7P
 83507-89-5P 84052-82-4P 89083-53-4P 103667-57-8P 103733-65-9P
 169390-26-5P 169390-27-6P 169820-06-8P 169820-07-9P 169820-08-0P
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 169820-14-8P 169820-15-9P 169820-16-0P 169820-17-1P 169820-18-2P
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 169820-29-5P 169820-30-8P 169820-31-9P 169820-32-0P 169820-33-1P
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 169820-39-7P 169820-40-0P 169820-41-1P 169820-42-2P 169820-43-3P
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 169820-54-6P **169820-55-7P 169820-56-8P**
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169820-60-4P 169820-61-5P 169820-62-6P 169820-63-7P
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 169820-74-0P 169820-75-1P 169820-76-2P **169820-77-3P**
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 169820-82-0P 169820-83-1P 169820-84-2P 169820-85-3P 169820-86-4P
 169820-87-5P 169820-88-6P 170079-02-4P 170079-03-5P 170079-04-6P
 170079-05-7P 170079-06-8P 170079-07-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(antithrombotic arginine aldehyde derivs.)

IT **169820-55-7P 169820-56-8P 169820-57-9P**
169820-58-0P 169820-60-4P 169820-61-5P
169820-77-3P 169820-78-4P

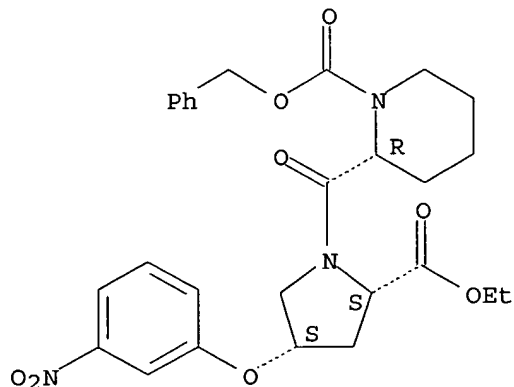
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(antithrombotic arginine aldehyde derivs.)

RN 169820-55-7 CAPLUS

CN 1-Piperidinecarboxylic acid, 2-[[2-(ethoxycarbonyl)-4-(3-nitrophenoxy)-1-
 pyrrolidinyl]carbonyl]-, phenylmethyl ester, [2S-
 [1(S*),2 α ,4 α]]- (9CI) (CA INDEX NAME)

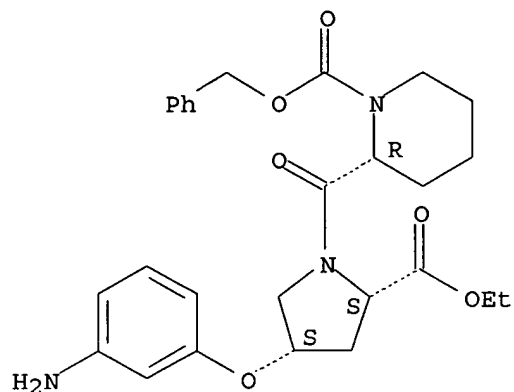
Absolute stereochemistry.



RN 169820-56-8 CAPLUS

CN 1-Piperidinecarboxylic acid, 2-[[4-(3-aminophenoxy)-2-(ethoxycarbonyl)-1-pyrrolidinyl]carbonyl]-, phenylmethyl ester, [2S-[1(S*),2 α ,4 α]]- (9CI) (CA INDEX NAME)

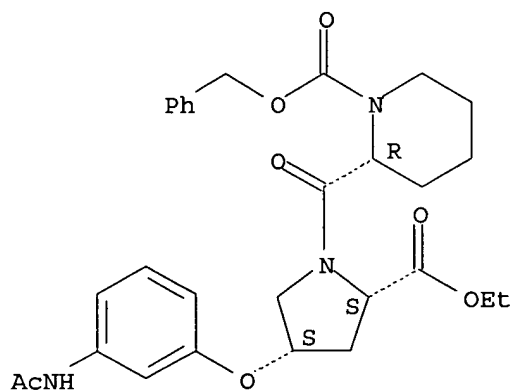
Absolute stereochemistry.



RN 169820-57-9 CAPLUS

CN 1-Piperidinecarboxylic acid, 2-[[4-[3-(acetylamino)phenoxy]-2-(ethoxycarbonyl)-1-pyrrolidinyl]carbonyl]-, phenylmethyl ester, [2S-[1(S*),2 α ,4 α]]- (9CI) (CA INDEX NAME)

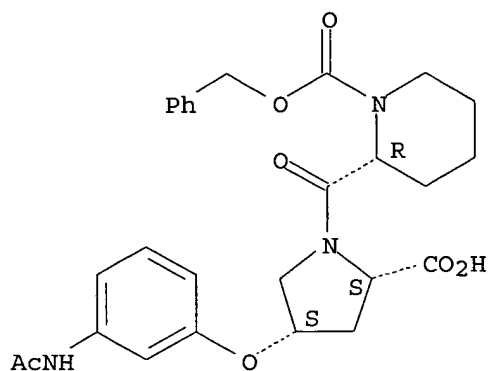
Absolute stereochemistry.



RN 169820-58-0 CAPLUS

CN 1-Piperidinecarboxylic acid, 2-[[4-[3-(acetylamino)phenoxy]-2-carboxy-1-pyrrolidinyl]carbonyl]-, 1-(phenylmethyl) ester, [2S-[1(S*),2 α ,4 α]]- (9CI) (CA INDEX NAME)

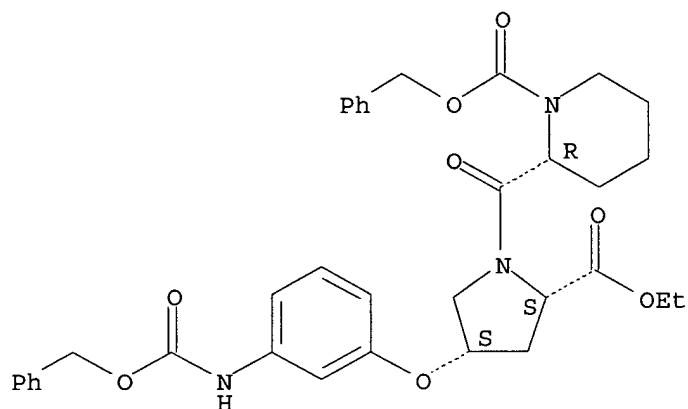
Absolute stereochemistry.



RN 169820-60-4 CAPLUS

CN 1-Piperidinecarboxylic acid, 2-[[2-(ethoxycarbonyl)-4-[3-
[[(phenylmethoxy) carbonyl] amino] phenoxy] -1-pyrrolidinyl] carbonyl] -,
phenylmethyl ester, [2S-[1(S*),2α,4α]]- (9CI) (CA INDEX NAME)

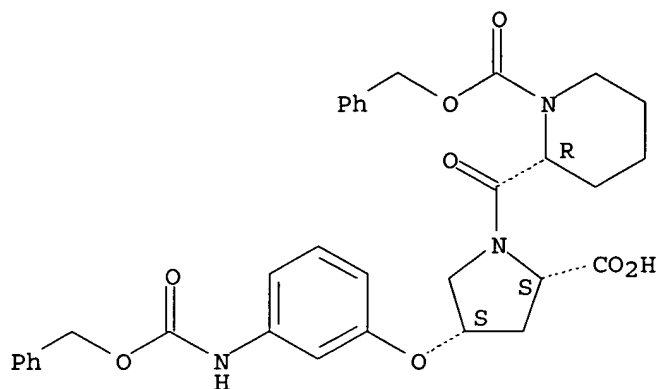
Absolute stereochemistry.



RN 169820-61-5 CAPLUS

CN 1-Piperidinecarboxylic acid, 2-[[2-carboxy-4-[3-
[[(phenylmethoxy) carbonyl] amino] phenoxy] -1-pyrrolidinyl] carbonyl] -,
1-(phenylmethyl) ester, [2S-[1(S*),2α,4α]]- (9CI) (CA INDEX
NAME)

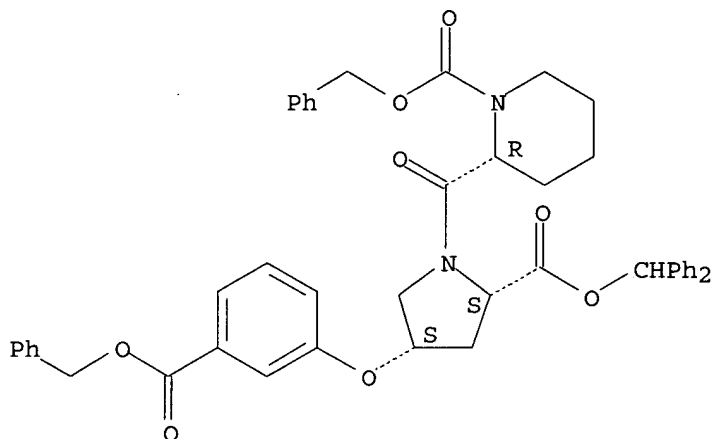
Absolute stereochemistry.



RN 169820-77-3 CAPLUS

CN 1-Piperidinecarboxylic acid, 2-[[2-[(diphenylmethoxy)carbonyl]-4-[3-[(phenylmethoxy)carbonyl]phenoxy]-1-pyrrolidinyl]carbonyl]-, phenylmethyl ester, [2S-[1(S*),2α,4α]]- (9CI) (CA INDEX NAME)

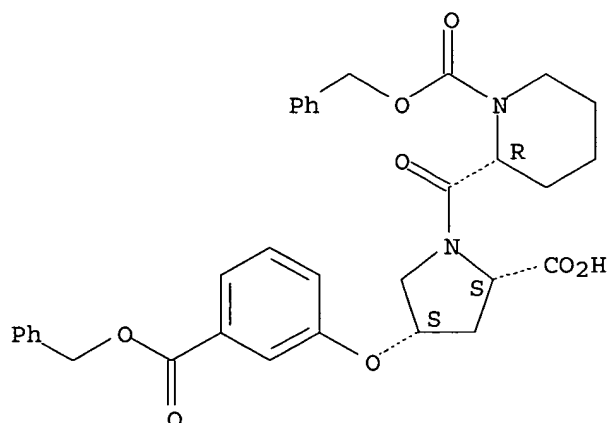
Absolute stereochemistry.



RN 169820-78-4 CAPLUS

CN 1-Piperidinecarboxylic acid, 2-[[2-carboxy-4-[3-[(phenylmethoxy)carbonyl]phenoxy]-1-pyrrolidinyl]carbonyl]-, 1-(phenylmethyl) ester, [2S-[1(S*),2α,4α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 48 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:896131 CAPLUS

DOCUMENT NUMBER: 123:314523

TITLE: Preparation of aspartic acid derivatives and homologs thereof for treatment of neurological diseases.

INVENTOR(S): Carrera, Jesus Ezquerra; Esteban, Almudena Rubio; Mann, Andre; Schoenfelder, Angele; Schoepp, Darryle Darwin; Tercero, Conception Pedregal; Wermuth, Camille-Georges

PATENT ASSIGNEE(S): Universite Louis Pasteur, Fr.; Lilly S.A.; Eli Lilly and Co.

SOURCE: Eur. Pat. Appl., 24 pp.

CODEN: EPXXDW

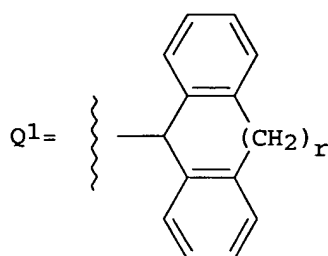
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 656345	A1	19950607	EP 1994-308952	19941202
EP 656345	B1	19990310		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2137028	AA	19950604	CA 1994-2137028	19941130
JP 08020564	A2	19960123	JP 1994-299206	19941202
AT 177419	E	19990315	AT 1994-308952	19941202
ES 2130370	T3	19990701	ES 1994-308952	19941202
PRIORITY APPLN. INFO.:			GB 1993-24872	A 19931203
OTHER SOURCE(S):	CASREACT 123:314523; MARPAT 123:314523			
GI				



AB Z(CH₂)_qYp(CH₂)_nCHX(CH₂)_mCH(NH₂)CO₂H [m = 0-2; n, q = 0-5; p = 0, 1; X = CO₂H, tetrazolyl; Y = CH:CH; Z = (substituted) Ph, naphthyl, thienyl, CHR₁R₂, :CR₁R₂, Q₁; R₁, R₂ = (substituted) Ph, naphthyl, thienyl; r = 0-3; provided that when Z = Ph and m = 1, then p = 1], were prepared as ligands for metabotropic glutamate receptors and blockers of metabotropic glutamate receptor second messenger responses. (2R, 4R,S)-2-amino-4-(3-phenyl-2-propenyl)-1,5-pentanedioic acid was prepared in several steps from (4R)-1,1-dimethylethyl-4-(3-ethoxy-3-oxopropenyl)-2,2-dimethyl-3-oxazolidinecarboxylate. Preferred I showed IC₅₀ <100 μm for selective displacement of (1S,3R)-ACPD in rat brain membranes.

IC ICM C07C229-36

ICS C07D257-04; A61K031-195; A61K031-41

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT **153080-90-1P 153080-94-5P 158512-77-7P 158512-78-8P**
 169338-02-7P 169338-09-4P 169756-48-3P 169756-49-4P 169756-50-7P
 169756-51-8P 169756-52-9P 169756-53-0P 169756-54-1P 169756-55-2P
 169756-56-3P 169756-57-4P 169756-58-5P 169756-59-6P 169756-60-9P
 169756-61-0P 169756-62-1P 169756-63-2P 169756-64-3P 169756-65-4P
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 169756-76-7P 169756-77-8P 169756-78-9P **169756-79-0P**
169756-80-3P 169756-81-4P 169756-82-5P 169756-83-6P
 169756-84-7P 169756-85-8P **169756-86-9P** 169756-87-0P
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 169756-98-3P 169756-99-4P 169757-00-0P 169757-01-1P 169757-02-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of aspartic acid derivs. and homologs thereof for treatment of neurol. diseases)

IT **153080-90-1P 153080-94-5P 169756-79-0P**

169756-80-3P 169756-86-9P

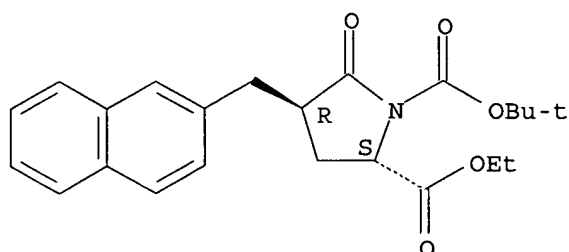
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of aspartic acid derivs. and homologs thereof for treatment of neurol. diseases)

RN 153080-90-1 CAPLUS

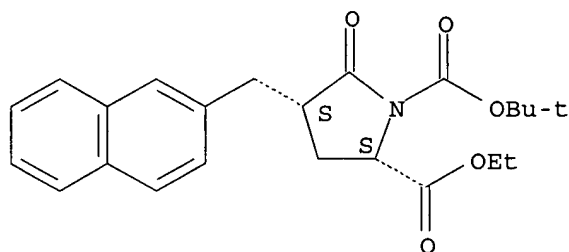
CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenylmethyl)-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



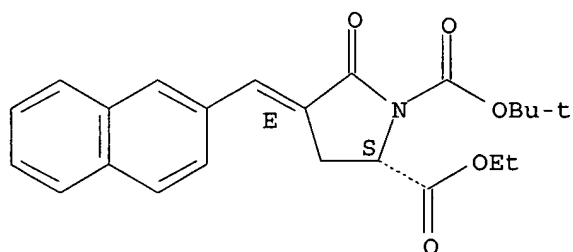
RN 153080-94-5 CAPLUS
 CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenylmethyl)-5-oxo-,
 1-(1,1-dimethylethyl) 2-ethyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



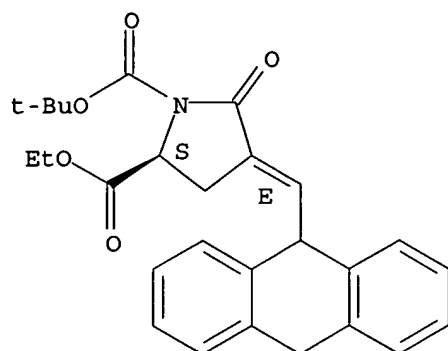
RN 169756-79-0 CAPLUS
 CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenylmethylene)-5-oxo-,
 1-(1,1-dimethylethyl) 2-ethyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 169756-80-3 CAPLUS
 CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(9,10-dihydro-9-anthracenyl)methylene]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester,
 [S-(E)]- (9CI) (CA INDEX NAME)

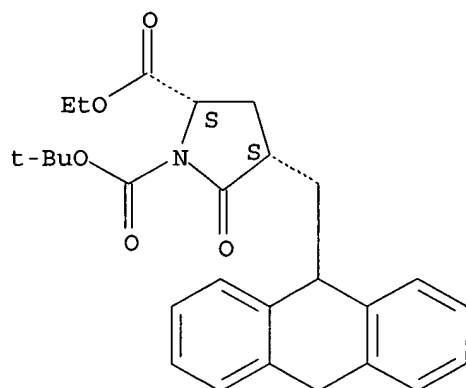
Absolute stereochemistry.
 Double bond geometry as shown.



RN 169756-86-9 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(9,10-dihydro-9-anthracenyl)methyl]-5-oxo-, 1-(1,1-dimethylethyl) 2-ethyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 49 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:835486 CAPLUS

DOCUMENT NUMBER: 123:257395

TITLE: Imidazolyl amino acid derivatives as angiotensin II antagonists

INVENTOR(S): Boyd, Donald B.; Hauser, Kenneth L.; Lifer, Sherryl L.; Marshall, Winston S.; Palkowitz, Alan D.; Pfeifer, William; Reel, Jon K.; Simon, Richard L.; Steinberg, Mitchell I.; et al.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: U.S., 29 pp. Cont.-in-part of U.S. Ser. No. 892,867, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5401851	A	19950328	US 1993-49917	19930420
CA 2097462	AA	19931204	CA 1993-2097462	19930601
HU 64328	A2	19931228	HU 1993-1603	19930601
IL 105877	A1	19980715	IL 1993-105877	19930601
NO 9302005	A	19931206	NO 1993-2005	19930602
EP 573271	A1	19931208	EP 1993-304264	19930602
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AU 9339985	A1	19940120	AU 1993-39985	19930602
AU 667903	B2	19960418		
RU 2110515	C1	19980510	RU 1993-46497	19930602
CN 1085897	A	19940427	CN 1993-107578	19930603
CN 1045768	B	19991020		
JP 07304752	A2	19951121	JP 1993-133212	19930603
PL 173340	B1	19980227	PL 1993-299176	19930603
US 5484780	A	19960116	US 1994-355778	19941214

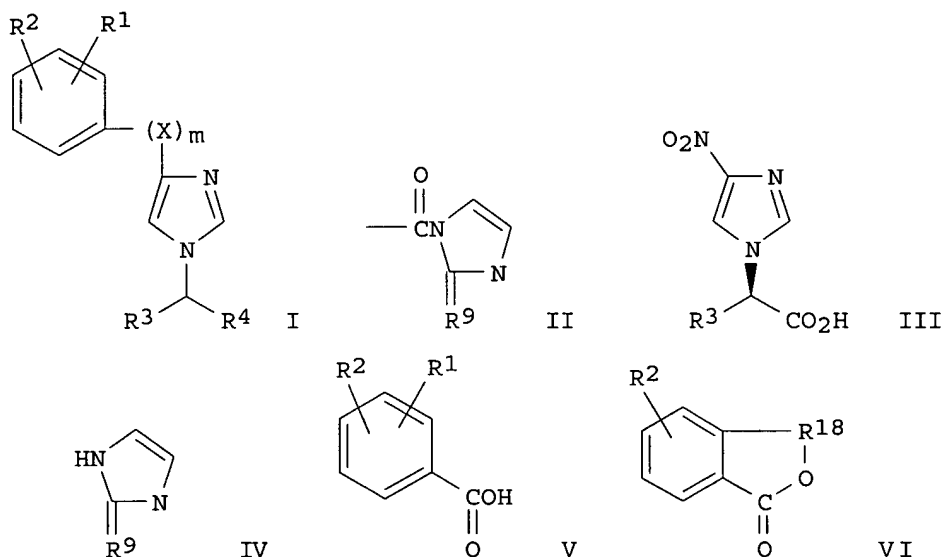
PRIORITY APPLN. INFO.:

US 1992-892867	B2	19920603
US 1993-49917	A	19930420

OTHER SOURCE(S):

CASREACT 123:257395; MARPAT 123:257395

GI



AB A process of preparing a substantially pure (R) enantiomer of the compound of the formula I wherein: R1 is CO₂H, SO₃H, PO₃H₂, CONHSO₂R₅ or 5-tetrazolyl; R2 is H, OH, OCOCH₃, halo, C₁-C₄ alkyl, amino, acetamido, or C₁-C₄ alkoxy; X is (CH₂)_mNHCO, (CH₂)_mCONH, O, NH, CH₂, (CH₂)_mCO, or CO(CH₂)_m; R3 is C₄-C₉ straight chain alkyl, C₄-C₉ straight chain trifluoroalkyl, C₄-C₉ straight chain alkenyl, or C₄-C₉ straight chain trifluoroalkenyl; R4 is CONH(C₁-C₄ alkyl), CONH(C₁-C₄ trifluoroalkyl), CONH(hydroxy-C₁-C₄ alkyl), or, e.g., II; R5 is Ph, C₁-C₄ alkyl substituted Ph, C₁-C₅ alkyl, or C₁-C₅ trifluoroalkyl; R9 is O or S; m is independently 0 or 1; p is independently 0, 1, 2, 3 or 4; and q is 1, 2, 3, or 4 (with provisos); comprising coupling a compound of the formula III to, e.g., IV; reducing the nitro of the compound of the formula III to produce an aminoimidazole; coupling the aminoimidazole to V or VI (R₁₈ = SO₂ or CO). Thus, e.g., reaction of 4-nitroimidazole with Et 2-bromooctanoate afforded Et

2-(4-nitro-1H-imidazol-1-yl)octanoate; reaction of the latter with ethylamine afforded N-ethyl-2-(4-nitro-1H-imidazol-1-yl)octanoamide; N-ethyl-2-(4-nitro-1H-imidazol-1-yl)octanoamide was reduced by hydrogenation at 40 psi over Pd/C and the aminoimidazole was added to a solution of 2-sulfobenzoic acid cyclic anhydride to afford N-ethyl-2-[4-(2-sulfobenzoyl)amino-1H-imidazol-1-yl]octanoamide (VII). The ability of I to block angiotensin II receptor binding (KI, μM) was determined using the adrenal glomerulosa assay, and the ability to antagonize angiotensin-induced vasoconstriction [potency = pA₂ (defined as -log KB, where KB = [molar concentration of antagonist]/[(EC₅₀ AII with antagonist/EC₅₀ AII without antagonist)-1])] was evaluated in the rabbit aorta test system: for VII, KI = 10.3 and pA₂ = 5.7. Pharmaceutical formulations were given.

IC ICM A61K031-415

ICS A61K031-44; A61K031-505; C07D233-58; C07D239-26; C07D213-06

INCL 548112000

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 63

IT 154668-27-6P 157176-72-2P 157176-73-3P 157176-74-4P 157176-75-5P
 157176-76-6P 157176-77-7P 157176-78-8P 157176-80-2P 157176-81-3P
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RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(imidazolyl amino acid derivs. as angiotensin II antagonists)

IT 81-08-3, 2-Sulfobenzoic acid cyclic anhydride 85-44-9,
 1,3-Isobenzofurandione 100-02-7, 4-Nitrophenol, reactions 100-51-6,
 Benzenemethanol, reactions 103-16-2, 4-Benzyloxyphenol 106-41-2,
 4-Bromophenol 107-10-8, Propylamine, reactions 108-95-2, Phenol,
 reactions 115-11-7, reactions 123-75-1, Pyrrolidine, reactions
 124-68-5, 2-Amino-2-methyl-1-propanol 141-97-9, Ethyl acetoacetate
 349-88-2 767-00-0, 4-Cyanophenol 814-49-3, Diethyl chlorophosphate
 836-42-0, 4-Benzyloxybenzyl chloride 1486-51-7, 4-Benzyloxybenzoic acid
 1660-94-2, Tetraethyl methylenediphosphonate 2133-40-6, L-Proline methyl
 ester hydrochloride 2623-82-7, 2-Bromooctanoic acid 3034-38-6,
 4-Nitroimidazole 4224-70-8, 6-Bromohexanoic acid 4397-53-9,
 4-Benzyloxybenzaldehyde 5445-29-4, Ethyl 2-bromooctanoate 6342-70-7,
 Methyl 2-hydroxy-3-methoxybenzoate 6373-46-2, 4-Benzyloxyaniline
 6793-92-6, 4-Benzyloxybromobenzene 13504-85-3 16420-13-6 16652-71-4,

L-Proline benzyl ester hydrochloride 37418-88-5, 3-Hydroxyphthalic anhydride 74844-91-0 154993-49-4 774221-29-3 774221-31-7
 774221-35-1 774221-37-3 774221-39-5 774223-25-5 774223-27-7
 774223-28-8 774223-29-9 774223-30-2 774223-41-5 774223-49-3
 774223-50-6 774223-52-8 774223-53-9 774224-65-6 774224-66-7
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 774225-61-5 774226-68-5 774227-02-0 774235-68-6 774576-11-3
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 774576-77-1 774577-12-7 774577-21-8
 774577-22-9 774577-31-0 774577-44-5 774577-45-6
 774577-46-7 774577-48-9

RL: RCT (Reactant); RACT (Reactant or reagent)
 (imidazolyl amino acid derivs. as angiotensin II antagonists)

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 157186-72-6P 157186-73-7P 157186-74-8P
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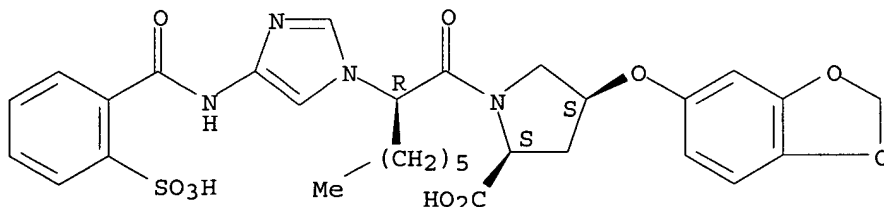
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(imidazolyl amino acid derivs. as angiotensin II antagonists)

RN 157186-69-1 CAPLUS

CN L-Proline, 4-(1,3-benzodioxol-5-yloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, hydrochloride (2:1), [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

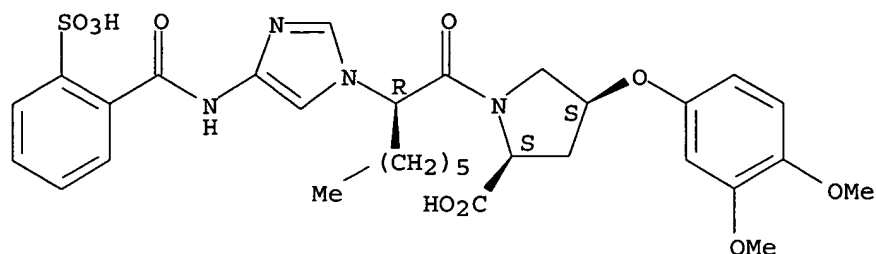


● 1/2 HCl

RN 157186-70-4 CAPLUS

CN L-Proline, 4-(3,4-dimethoxyphenoxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, hydrochloride (2:1), [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

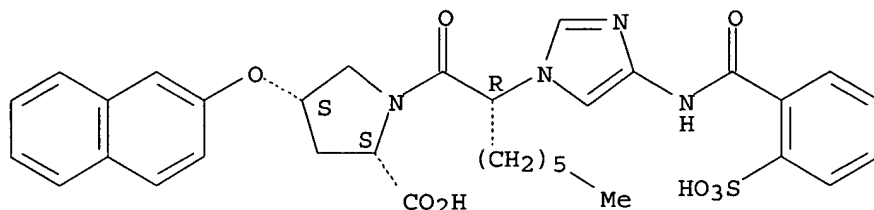


● 1/2 HCl

RN 157186-71-5 CAPLUS

CN L-Proline, 4-(2-naphthalenyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

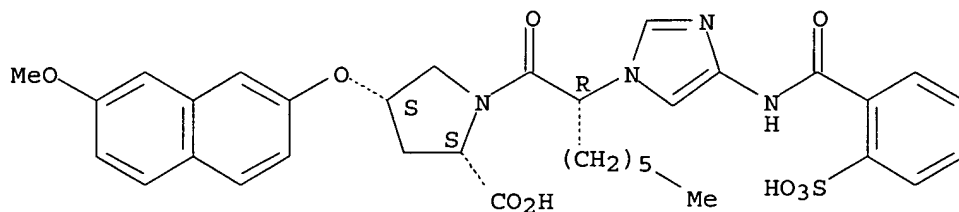
Absolute stereochemistry.



RN 157186-72-6 CAPLUS

CN L-Proline, 4-[(7-methoxy-2-naphthalenyl)oxy]-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

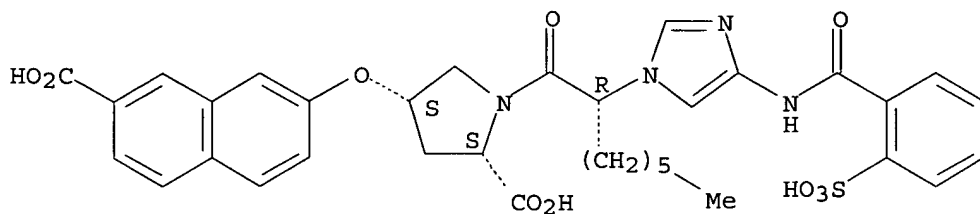
Absolute stereochemistry.



RN 157186-73-7 CAPLUS

CN L-Proline, 4-[(7-carboxy-2-naphthalenyl)oxy]-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

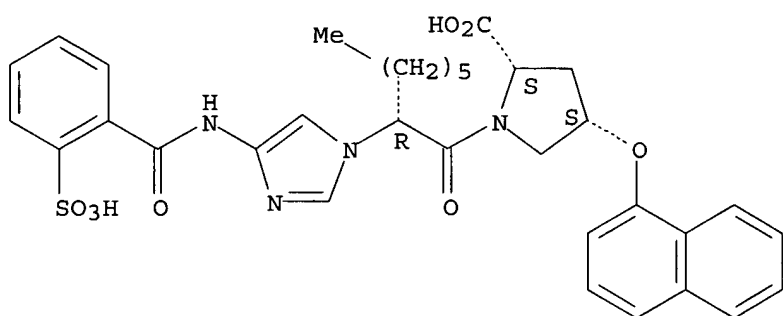
Absolute stereochemistry.



RN 157186-74-8 CAPLUS

CN L-Proline, 4-(1-naphthalenyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

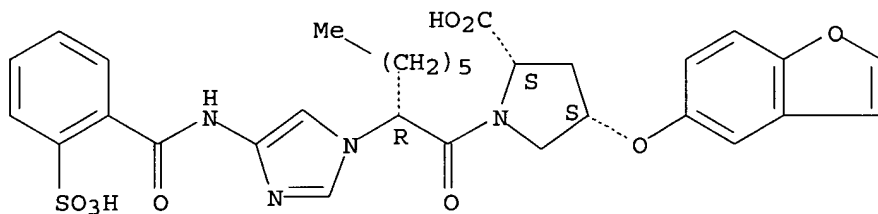
Absolute stereochemistry.



RN 157186-75-9 CAPLUS

CN L-Proline, 4-(5-benzofuranyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, monohydrochloride, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

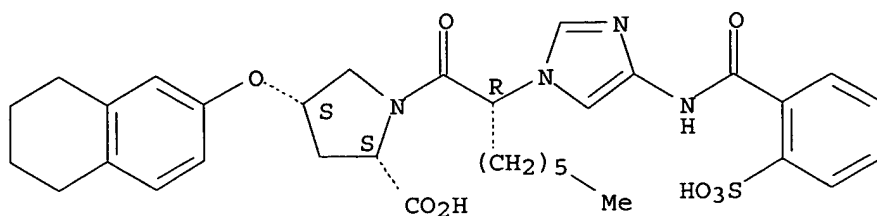


● HCl

RN 157186-76-0 CAPLUS

CN L-Proline, 1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-4-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]-, monohydrochloride, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

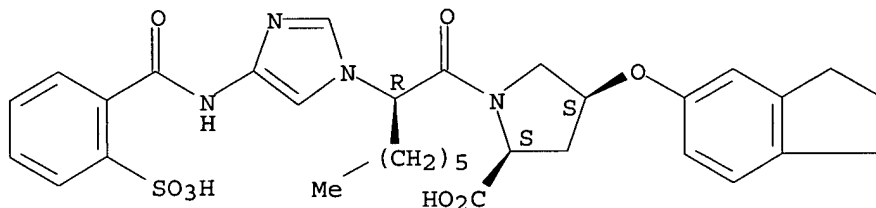


● HCl

RN 157186-77-1 CAPLUS

CN L-Proline, 4-[(2,3-dihydro-1H-inden-5-yl)oxy]-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, hydrochloride (5:3), [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

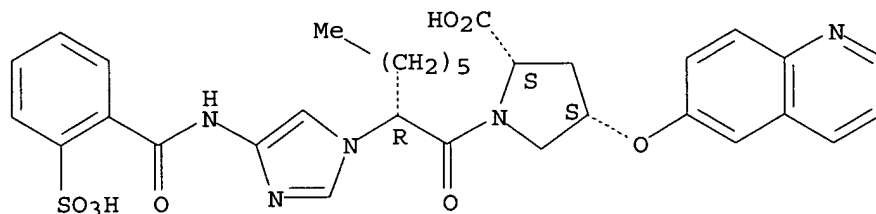


● 3/5 HCl

RN 157186-78-2 CAPLUS

CN L-Proline, 1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-4-(6-quinolinyloxy)-, hydrochloride (5:6), [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



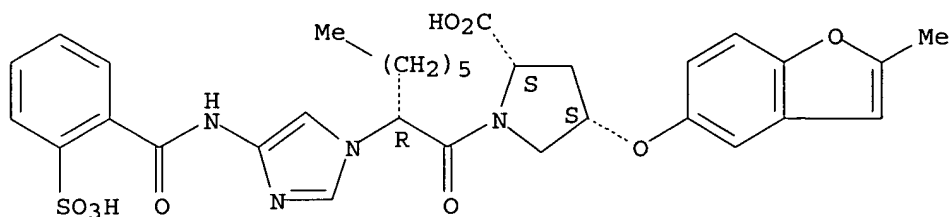
● 6/5 HCl

RN 157186-79-3 CAPLUS

CN L-Proline, 4-[(2-methyl-5-benzofuranyl)oxy]-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, hydrochloride (2:1),

[1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

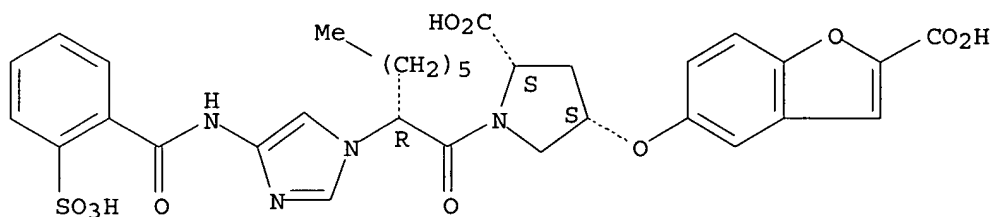


● 1/2 HCl

RN 157186-80-6 CAPLUS

CN L-Proline, 4-[(2-carboxy-5-benzofuranyl)oxy]-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

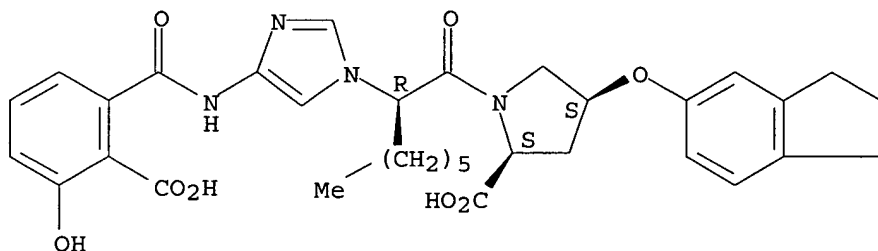
Absolute stereochemistry.



RN 157186-97-5 CAPLUS

CN L-Proline, 1-[2-[4-[(2-carboxy-3-hydroxybenzoyl)amino]-1H-imidazol-1-yl]-1-oxooctyl]-4-[(2,3-dihydro-1H-inden-5-yl)oxy]-, hydrochloride (4:3), [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



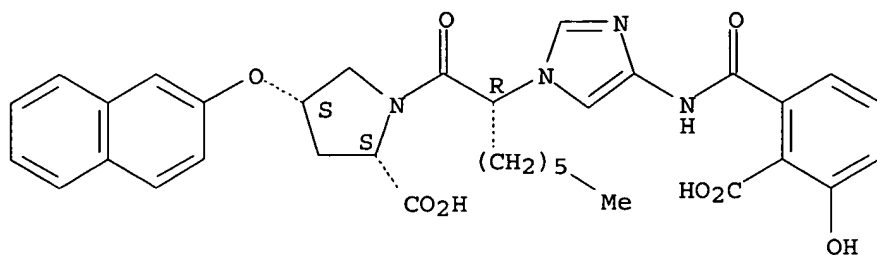
● 3/4 HCl

RN 157186-98-6 CAPLUS

CN L-Proline, 1-[2-[4-[(2-carboxy-3-hydroxybenzoyl)amino]-1H-imidazol-1-yl]-1-oxooctyl]-4-(2-naphthalenyloxy)-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

INDEX NAME)

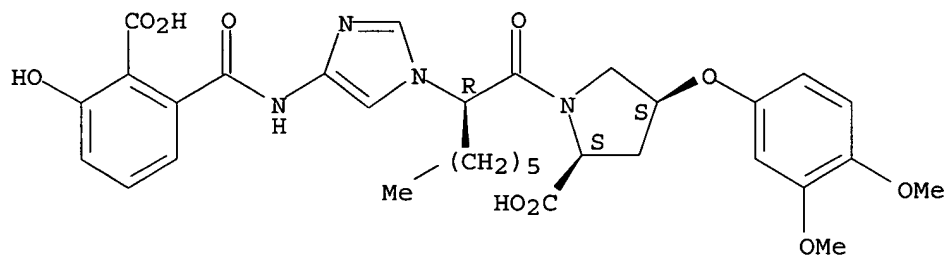
Absolute stereochemistry.



RN 157186-99-7 CAPLUS

CN L-Proline, 1-[2-[4-[(2-carboxy-3-hydroxybenzoyl)amino]-1H-imidazol-1-yl]-1-oxooctyl]-4-(3,4-dimethoxyphenoxy)-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

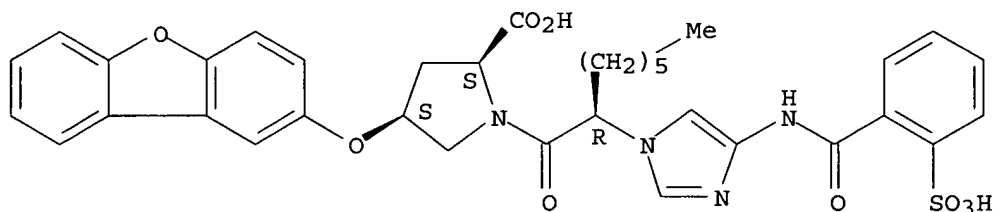
Absolute stereochemistry.



RN 168750-84-3 CAPLUS

CN L-Proline, 4-(2-dibenzofuranyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, monohydrochloride, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

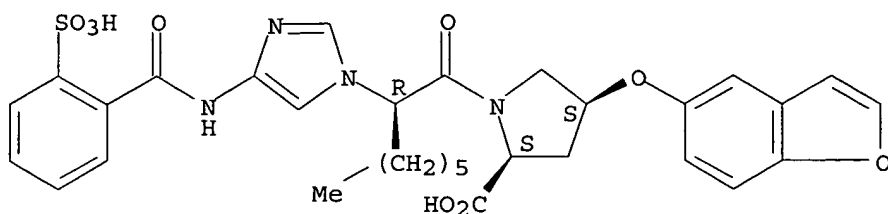


● HCl

RN 168750-85-4 CAPLUS

CN L-Proline, 4-(5-benzofuranyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, hydrochloride (2:7), [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 7/2 HCl

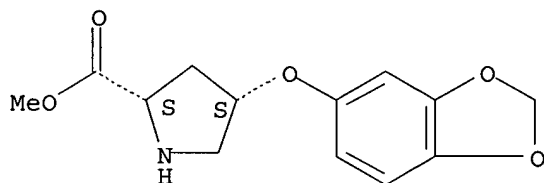
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 774577-21-8 774577-22-9 774577-31-0

RL: RCT (Reactant); RACT (Reactant or reagent)
 (imidazolyl amino acid derivs. as angiotensin II antagonists)

RN 774576-62-4 CAPLUS

CN L-Proline, 4-(1,3-benzodioxol-5-yloxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

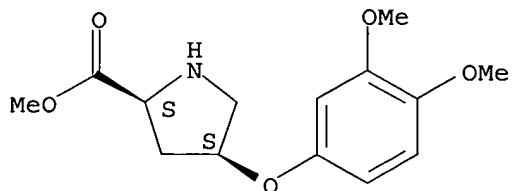
Absolute stereochemistry.



RN 774576-63-5 CAPLUS

CN L-Proline, 4-(3,4-dimethoxyphenoxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

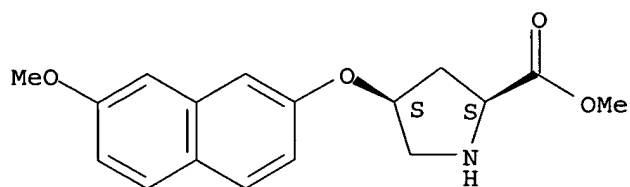
Absolute stereochemistry.



RN 774576-65-7 CAPLUS

CN L-Proline, 4-[(7-methoxy-2-naphthalenyl)oxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

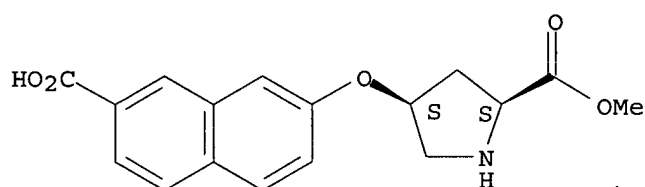
Absolute stereochemistry.



RN 774576-72-6 CAPLUS

CN L-Proline, 4-[(7-carboxy-2-naphthalenyl)oxy]-, 2-methyl ester, (4S)- (9CI)
(CA INDEX NAME)

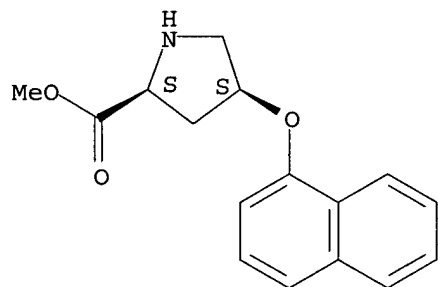
Absolute stereochemistry.



RN 774576-73-7 CAPLUS

CN L-Proline, 4-(1-naphthalenyloxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

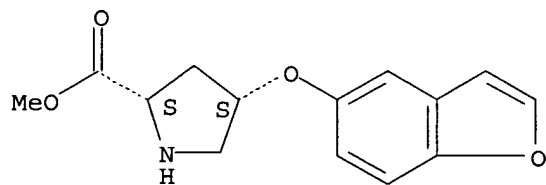
Absolute stereochemistry.



RN 774576-74-8 CAPLUS

CN L-Proline, 4-(5-benzofuranyloxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

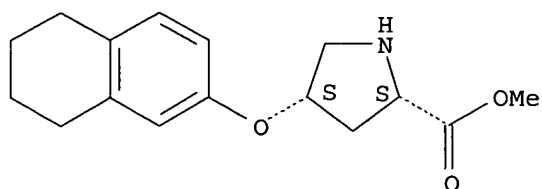


RN 774576-75-9 CAPLUS

CN L-Proline, 4-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]-, methyl ester,

(4S) - (9CI) (CA INDEX NAME)

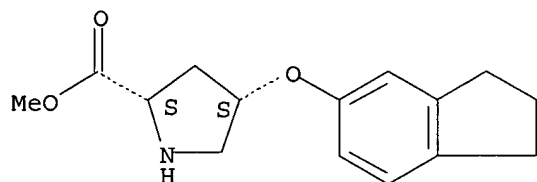
Absolute stereochemistry.



RN 774576-77-1 CAPLUS

CN L-Proline, 4-[(2,3-dihydro-1H-inden-5-yl)oxy]-, methyl ester, (4S) - (9CI)
(CA INDEX NAME)

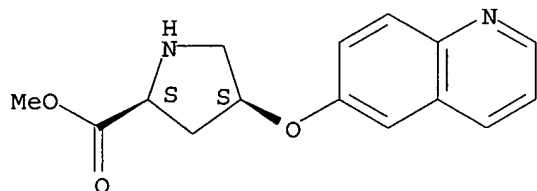
Absolute stereochemistry.



RN 774577-12-7 CAPLUS

CN L-Proline, 4-(6-quinolinyloxy)-, methyl ester, (4S) - (9CI) (CA INDEX
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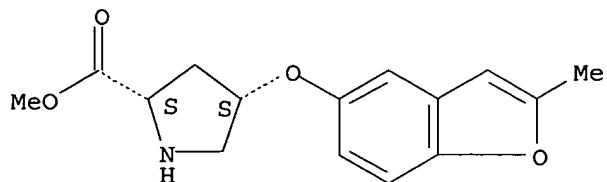
Absolute stereochemistry.



RN 774577-21-8 CAPLUS

CN L-Proline, 4-[(2-methyl-5-benzofuranyl)oxy]-, methyl ester, (4S) - (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

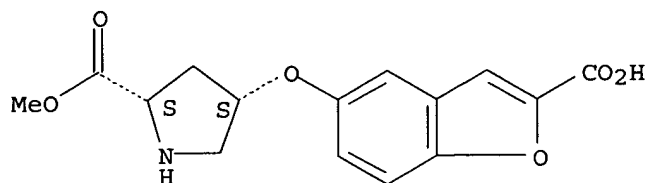


RN 774577-22-9 CAPLUS

CN L-Proline, 4-[(2-carboxy-5-benzofuranyl)oxy]-, 2-methyl ester, (4S) - (9CI)

(CA INDEX NAME)

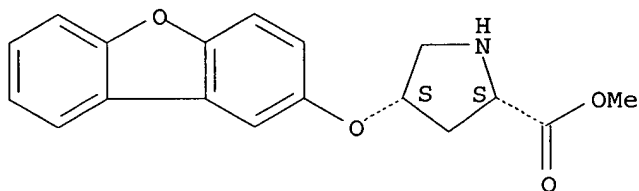
Absolute stereochemistry.



RN 774577-31-0 CAPLUS

CN L-Proline, 4-(2-dibenzofuranyloxy)-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 50 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:217324 CAPLUS

DOCUMENT NUMBER: 123:56516

TITLE: Structural Evolution and Pharmacology of a Novel Series of Triacid Angiotensin II Receptor Antagonists
 AUTHOR(S): Palkowitz, Alan D.; Steinberg, Mitchell I.; Thrasher, K. Jeff; Reel, Jon K.; Hauser, Kenneth L.; Zimmerman, Karen M.; Wiest, Sally A.; Whitesitt, Celia A.; Simon, Richard L.; et al.

CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA

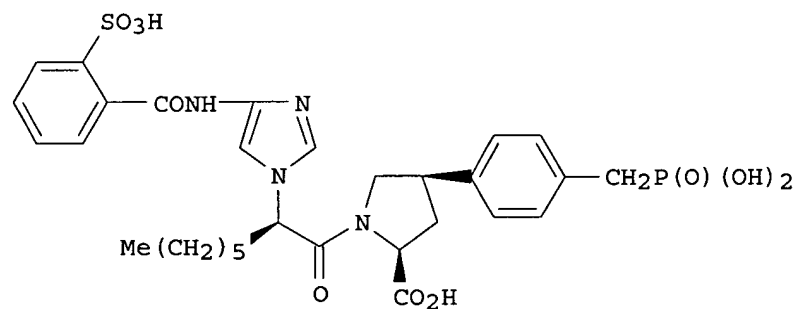
SOURCE: Journal of Medicinal Chemistry (1994), 37(26), 4508-21
 CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB Cis-4-(4-Phenoxy)-1-[1-oxo-2(R)-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-L-proline derivs. represent a novel class of potent nonpeptide angiotensin II (Ang II) receptor antagonists. These compds. evolved from directed structure-activity relationship (SAR) studies on a lead identified by random screening. Further SAR studies revealed that acidic modification of the 4-phenoxy ring system produced a series of triacid derivs. possessing oral activity in pithed rats. The most potent compound, I, inhibited the pressor response to exogenously administered Ang II for periods up to 8 h following oral dosing. The antihypertensive activity of I was evaluated in the lasix-pretreated conscious spontaneously hypertensive rat (SHR) where it produced a dose-dependent fall in blood pressure following oral dosing lasting >12 h. Antagonists such as I may serve as useful therapeutic agents for the treatment of hypertension as well as for studying the role of Ang II in various disease states.

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT 154668-27-6P 157176-84-6P 157176-88-0P 157176-92-6P 157176-93-7P
 157176-94-8P 157176-96-0P 157176-97-1P 157176-99-3P 157177-00-9P
 157177-01-0P 157177-05-4P 157177-08-7P 157177-16-7P 157186-62-4P
157186-71-5P 157186-74-8P 157187-00-3P 157241-15-1P
 164334-08-1P 164334-09-2P 164334-10-5P **164334-11-6P**
164334-12-7P 164334-13-8P 164334-14-9P
164334-15-0P 164334-16-1P 164455-50-9P 164455-51-0P
164455-52-1P 164455-53-2P 164455-54-3P
164455-55-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of sulfobenzoylaminoimidazolyloctanoylproline angiotensin II antagonists)

IT **157186-71-5P 157186-74-8P 164334-11-6P**
164334-12-7P 164334-13-8P 164334-15-0P
164334-16-1P 164455-52-1P 164455-53-2P
164455-54-3P 164455-55-4P

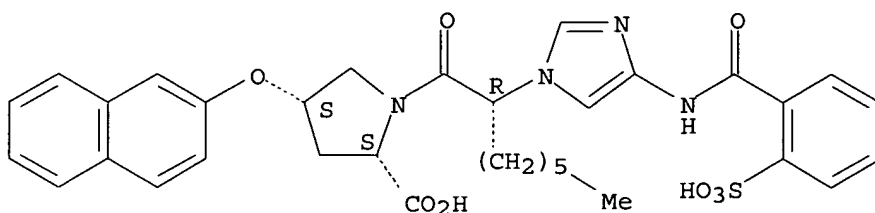
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of sulfobenzoylaminoimidazolyloctanoylproline angiotensin II antagonists)

RN 157186-71-5 CAPLUS

CN L-Proline, 4-(2-naphthalenyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

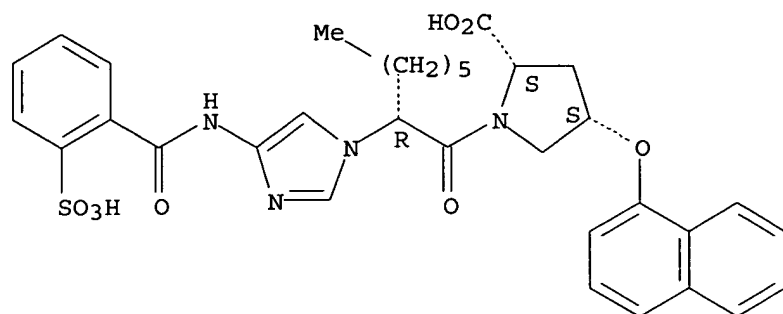
Absolute stereochemistry.



RN 157186-74-8 CAPLUS

CN L-Proline, 4-(1-naphthalenyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

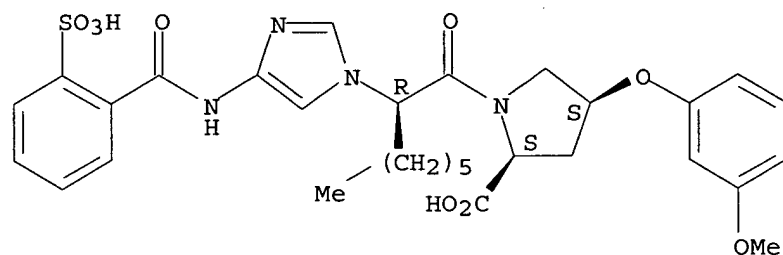
Absolute stereochemistry.



RN 164334-11-6 CAPLUS

CN L-Proline, 4-(3-methoxyphenoxy)-1-[(2R)-1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, (4S)- (9CI) (CA INDEX NAME)

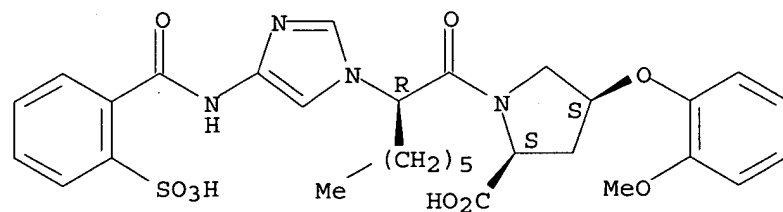
Absolute stereochemistry.



RN 164334-12-7 CAPLUS

CN L-Proline, 4-(2-methoxyphenoxy)-1-[(2R)-1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, (4S)- (9CI) (CA INDEX NAME)

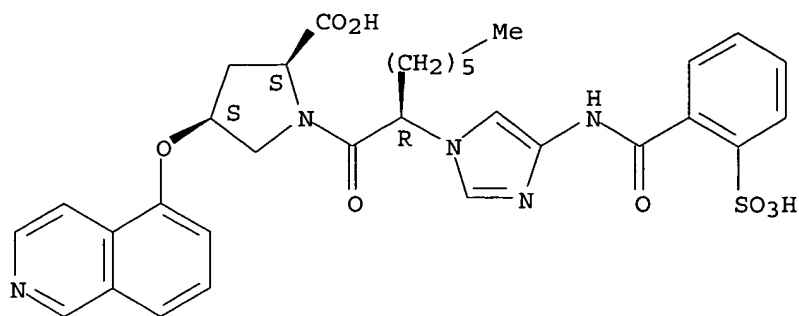
Absolute stereochemistry.



RN 164334-13-8 CAPLUS

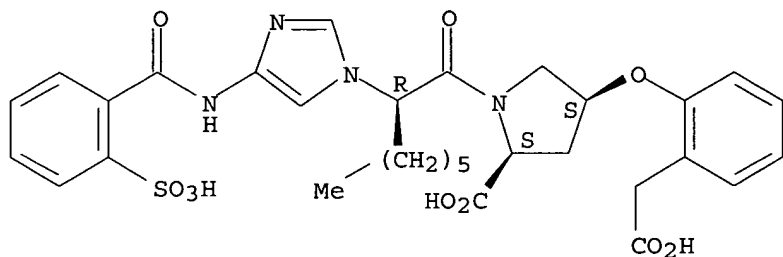
CN L-Proline, 4-(5-isoquinolinyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2α,4α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



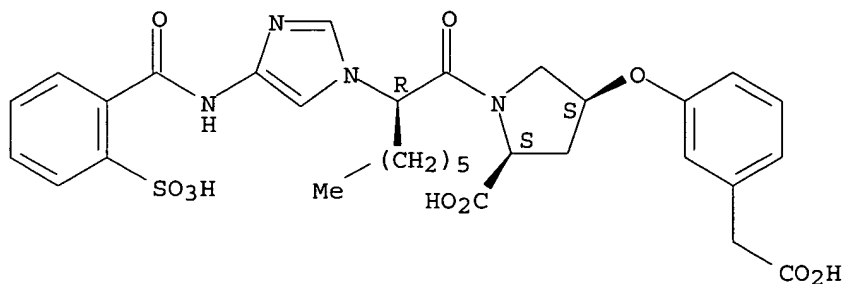
CN L-Proline, 4-[2-(carboxymethyl)phenoxy]-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



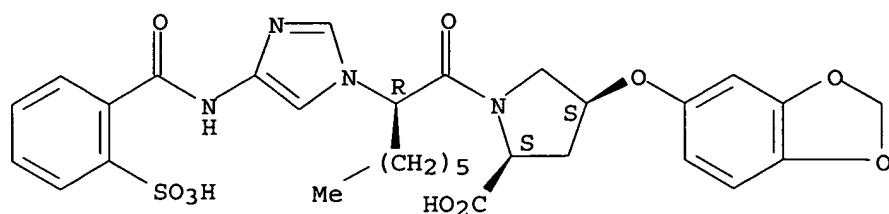
CN L-Proline, 4-[3-(carboxymethyl)phenoxy]-1-[1-oxo-2-[4-[(2-sulfo benzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



CN L-Proline, 4-(1,3-benzodioxol-5-yloxy)-1-[1-oxo-2-[4-[(2-sulfo benzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]-
(9CI) (CA INDEX NAME)

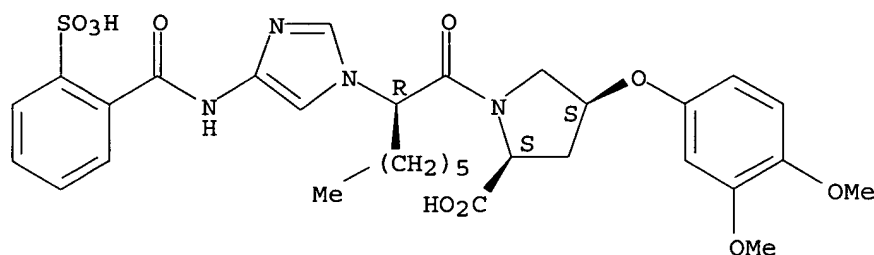
Absolute stereochemistry.



RN 164455-53-2 CAPLUS

CN L-Proline, 4-(3,4-dimethoxyphenoxy)-1-[(2R)-1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, (4S)- (9CI) (CA INDEX NAME)

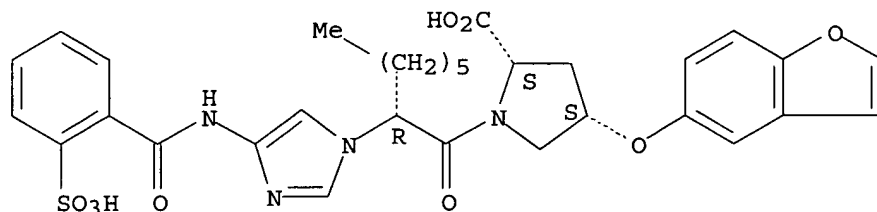
Absolute stereochemistry.



RN 164455-54-3 CAPLUS

CN L-Proline, 4-(5-benzofuranyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

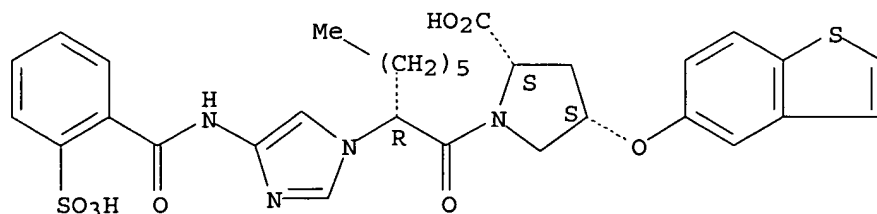
Absolute stereochemistry.



RN 164455-55-4 CAPLUS

CN L-Proline, 4-(benzo[b]thien-5-yloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

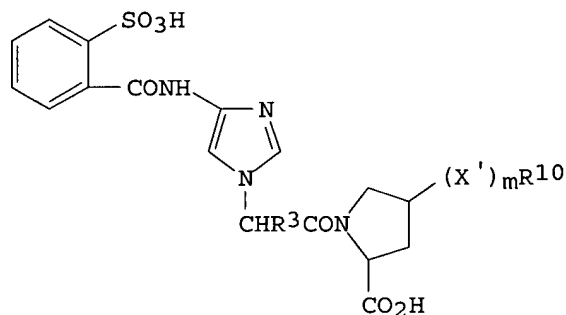
Absolute stereochemistry.



L47 ANSWER 51 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:558192 CAPLUS
 DOCUMENT NUMBER: 121:158192
 TITLE: Preparation of heterocyclyl-substituted L-proline as
 angiotensin II antagonists
 INVENTOR(S): Boyd, Donald Bradford; Hauser, Kenneth Lee; Lifer,
 Sherryl Lynn; Marshall, Winston Stanley; Palkowitz,
 Alan David; Pfeifer, William; Reel, Jon Kevin; Simon,
 Richard Lee; Steinberg, Mitchell Irvin; et al.
 PATENT ASSIGNEE(S): Eli Lilly and Co., USA
 SOURCE: Eur. Pat. Appl., 56 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 573271	A1	19931208	EP 1993-304264	19930602
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5401851	A	19950328	US 1993-49917	19930420
PRIORITY APPLN. INFO.:			US 1992-892867	A 19920603
			US 1993-49917	A 19930420
OTHER SOURCE(S):		MARPAT 121:158192		
GI				



AB Title compds. I [R3 = C4-9 alkyl; R10 = p-(substituted) Ph, (substituted) fused bicycyl or fused tricycyl; m = 0,1; X' = O, S (CH2)p wherein p = 0-4] or a salt thereof, are prepared (Me2CH)2NEt was added to D-proline benzyl ester-HCl in DMF followed by 2-(4-nitro-1H-imidazol-1-yl)octanoic acid to give a mixt of isomer esters which were reduced in EtOH with Pd/C, the catalyst filtered and to the product amine in THF was added sulfobenzoic anhydride to give D-I [R3 = C6H13, (X')mR10 is null] as 2 isomers (II). The ability to antagonize angiotensin-induced vasoconstriction was evaluated in rabbit aorta test system where the pA2 of II was 6.6 and 6.7. A number of imidazolyl derivs. were also prepared and evaluated. Pharmaceutical formulation of I are given.

IC ICM C07D233-88
 ICS C07D401-06; C07D401-14; C07D403-06; C07D403-14; C07D405-14;
 C07D409-14; C07D413-14; A61K031-41

CC 34-2 (Amino Acids, Peptides, and Proteins)
 Section cross-reference(s): 1, 28, 63

IT 154668-27-6P 157176-72-2P 157176-73-3P 157176-74-4P 157176-75-5P
 157176-76-6P 157176-77-7P 157176-78-8P 157176-79-9P 157176-80-2P
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 157241-15-1P 157241-16-2P 157241-17-3P 157241-18-4P 157241-19-5P
 157241-33-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of, as angiotensin II antagonist)

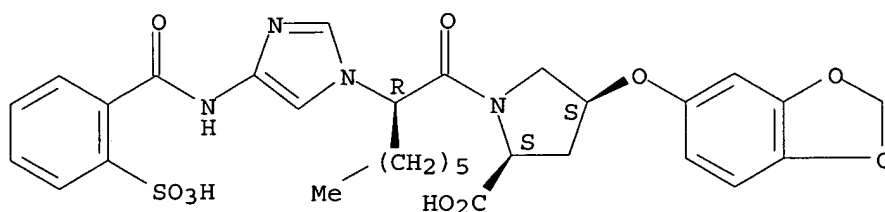
IT 157186-69-1P 157186-70-4P 157186-71-5P
 157186-72-6P 157186-73-7P 157186-74-8P
 157186-75-9P 157186-76-0P 157186-77-1P
 157186-78-2P 157186-79-3P 157186-80-6P
 157186-81-7P 157186-82-8P 157186-97-5P
 157186-98-6P 157186-99-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of, as angiotensin II antagonist)

RN 157186-69-1 CAPLUS

CN L-Proline, 4-(1,3-benzodioxol-5-yloxy)-1-[1-oxo-2-[4-[(2-sulfo benzoyl)amino]-1H-imidazol-1-yl]octyl]-, hydrochloride (2:1), [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

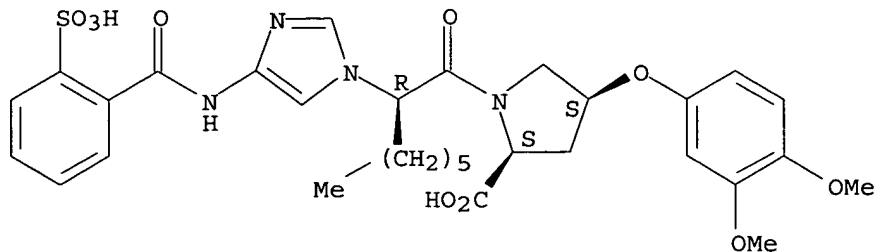


● 1/2 HCl

RN 157186-70-4 CAPLUS

CN L-Proline, 4-(3,4-dimethoxyphenoxy)-1-[1-oxo-2-[4-[(2-sulfo benzoyl)amino]-

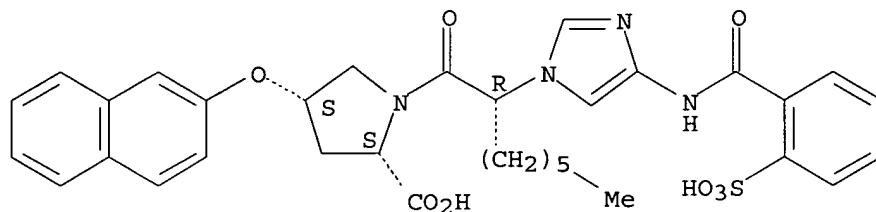
Absolute stereochemistry.



●_{1/2} HCl

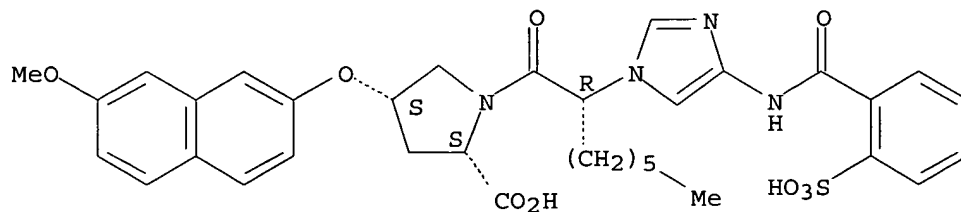
CN L-Proline, 4-(2-naphthalenyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



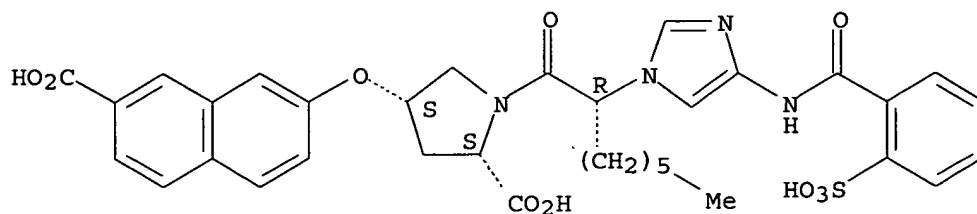
CN L-Proline, 4-[(7-methoxy-2-naphthalenyl)oxy]-1-[1-oxo-2-[4-[(2-sulfo benzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



CN L-Proline, 4-[(7-carboxy-2-naphthalenyl)oxy]-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]-
(9CI) (CA INDEX NAME)

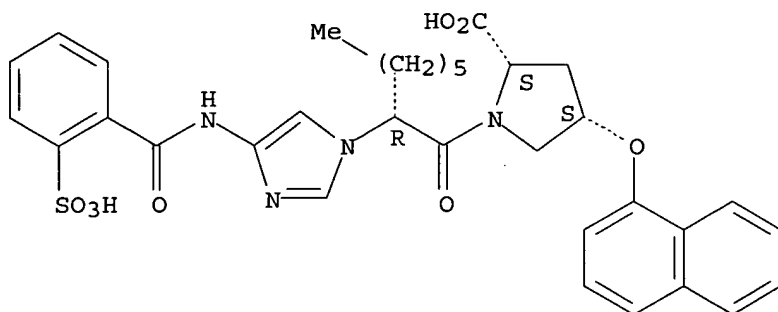
Absolute stereochemistry.



RN 157186-74-8 CAPLUS

CN L-Proline, 4-(1-naphthalenyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

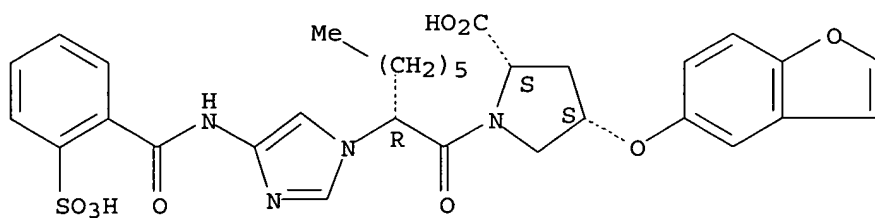
Absolute stereochemistry.



RN 157186-75-9 CAPLUS

CN L-Proline, 4-(5-benzofuranyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, monohydrochloride, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

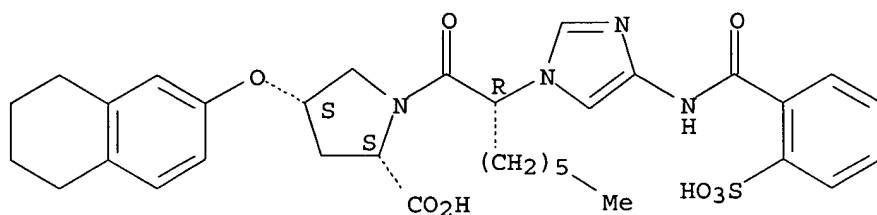


● HCl

RN 157186-76-0 CAPLUS

CN L-Proline, 1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-4-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]-, monohydrochloride, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

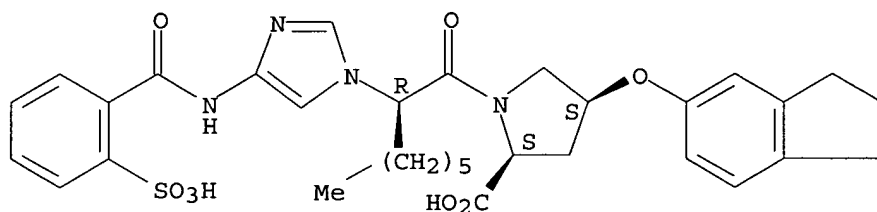


● HCl

RN 157186-77-1 CAPLUS

CN L-Proline, 4-[(2,3-dihydro-1H-inden-5-yl)oxy]-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, hydrochloride (5:3), [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

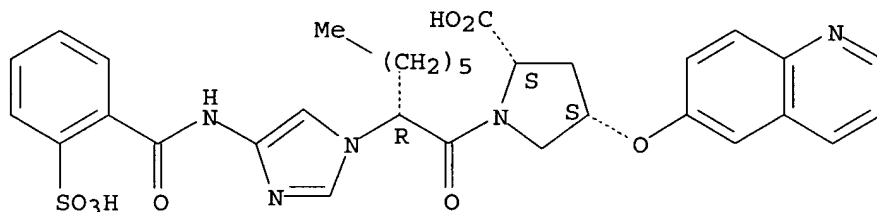


● 3/5 HCl

RN 157186-78-2 CAPLUS

CN L-Proline, 1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-4-(6-quinolinyloxy)-, hydrochloride (5:6), [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



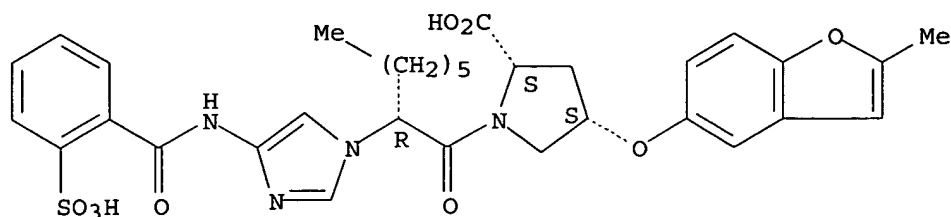
● 6/5 HCl

RN 157186-79-3 CAPLUS

CN L-Proline, 4-[(2-methyl-5-benzofuranyl)oxy]-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, hydrochloride (2:1),

[1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

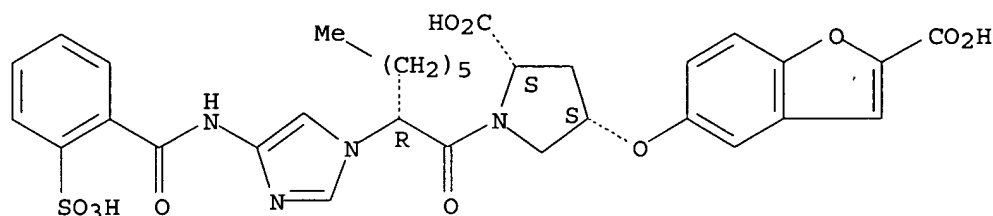


● 1/2 HCl

RN 157186-80-6 CAPLUS

CN L-Proline, 4-[(2-carboxy-5-benzofuranyl)oxy]-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

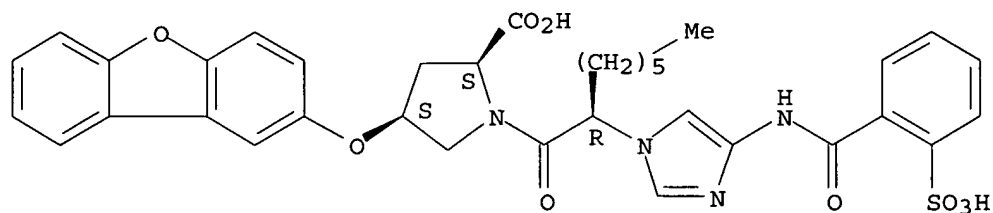
Absolute stereochemistry.



RN 157186-81-7 CAPLUS

CN L-Proline, 4-(2-dibenzofuranyloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, hydrochloride (2:1), [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

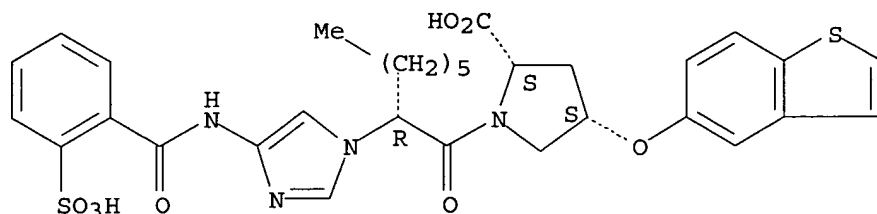


● 1/2 HCl

RN 157186-82-8 CAPLUS

CN L-Proline, 4-(benzo[b]thien-5-yloxy)-1-[1-oxo-2-[4-[(2-sulfobenzoyl)amino]-1H-imidazol-1-yl]octyl]-, hydrochloride (2:7), [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

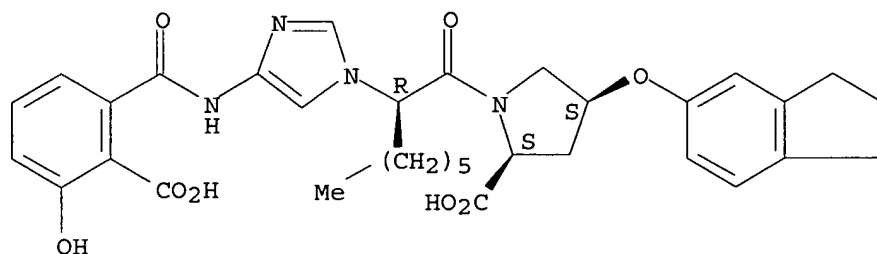


● 7/2 HCl

RN 157186-97-5 CAPLUS

CN L-Proline, 1-[2-[4-[(2-carboxy-3-hydroxybenzoyl)amino]-1H-imidazol-1-yl]-1-oxooctyl]-4-[(2,3-dihydro-1H-inden-5-yl)oxy]-, hydrochloride (4:3), [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

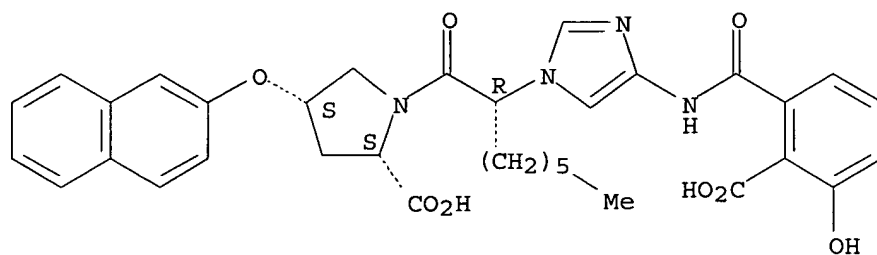


● 3/4 HCl

RN 157186-98-6 CAPLUS

CN L-Proline, 1-[2-[4-[(2-carboxy-3-hydroxybenzoyl)amino]-1H-imidazol-1-yl]-1-oxooctyl]-4-(2-naphthalenyloxy)-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

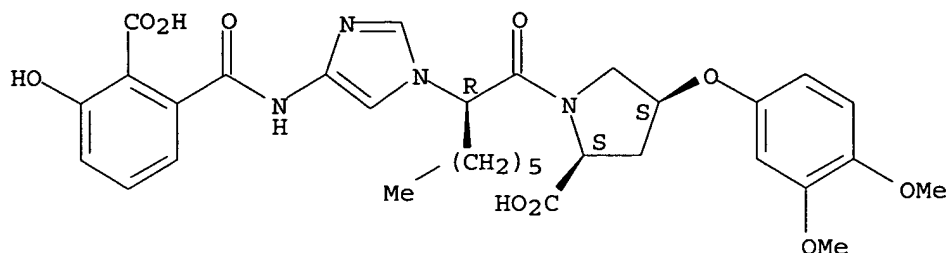


RN 157186-99-7 CAPLUS

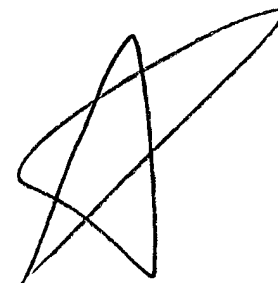
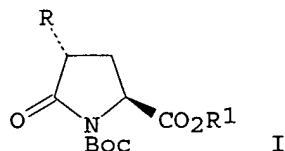
CN L-Proline, 1-[2-[4-[(2-carboxy-3-hydroxybenzoyl)amino]-1H-imidazol-1-yl]-1-oxooctyl]-4-(3,4-dimethoxyphenoxy)-, [1(S*),2 α ,4 α]- (9CI) (CA INDEX NAME)

INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 52 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1994:135094 CAPLUS
 DOCUMENT NUMBER: 120:135094
 TITLE: Stereoselective reactions of lithium enolates derived
 from N-BOC protected pyroglutamic esters
 AUTHOR(S): Ezquerria, Jesus; Pedregal, Concepcion; Rubio,
 Almudena; Yruretagoyena, Belen; Escribano, Ana;
 Sanchez-Ferrando, Francisco
 CORPORATE SOURCE: Cent. Invest. Lilly, S. A., Valdeolmos, 28130, Spain
 SOURCE: Tetrahedron (1993), 49(38), 8665-78
 CODEN: TETRAB; ISSN: 0040-4020
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 120:135094
 GI



AB The lithium enolates of protected pyroglutamate esters I (R = H, R1 = Et, CMe3; Boc = Me3CO2C) react with electrophiles in good yield without epimerization of the chiral center. With benzyl bromides the process is stereospecific, yielding exclusively trans isomers I (R = PhCH2, 4-MeC6H4CH2, 4-CF3C6H4CH2, 4-BrC6H4CH2, 4-NCC6H4CH2, 2-naphthylmethyl). However, with other reactive electrophiles a 2:1 trans/cis diastereomeric mixture was obtained, regardless of the steric bulk of the ester group.

CC 34-2 (Amino Acids, Peptides, and Proteins)

IT 153080-85-4P 153080-88-7P **153080-90-1P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and epimerization of, with cyanide)

IT 153080-67-2P 153080-68-3P 153080-69-4P 153080-70-7P 153080-71-8P
 153080-72-9P 153080-73-0P 153080-74-1P 153080-75-2P 153080-76-3P
 153080-77-4P 153080-78-5P 153080-79-6P 153080-80-9P 153080-81-0P
 153080-82-1P 153080-83-2P 153080-84-3P 153080-86-5P 153080-87-6P
 153080-89-8P 153080-92-3P 153080-93-4P **153080-94-5P**
 RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)

IT 153080-90-1P

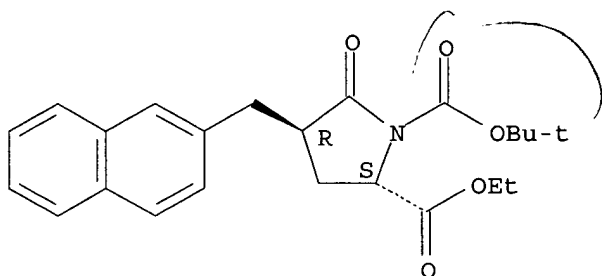
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation and epimerization of, with cyanide)

RN 153080-90-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenylmethyl)-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



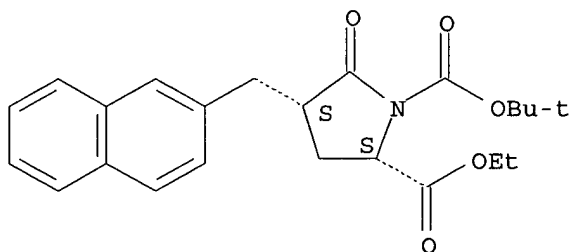
IT 153080-94-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 153080-94-5 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenylmethyl)-5-oxo-,
1-(1,1-dimethylethyl) 2-ethyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 53 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:517824 CAPLUS

DOCUMENT NUMBER: 119:117824

TITLE: Preparation of bradykinin antagonist peptides

INVENTOR(S): Kyle, Donald James; Hiner, Roger Neal

PATENT ASSIGNEE(S): Nova Technology L. P., USA

SOURCE: PCT Int. Appl., 142 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9218156	A1	19921029	WO 1992-US3033	19920416
W: AU, CA, FI, JP, KR, NO				

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE

AU 9218739	A1	19921117	AU 1992-18739	19920416
EP 618810	A1	19941012	EP 1992-917374	19920416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 07504155	T2	19950511	JP 1992-510290	19920416
CA 2106762	C	20001010	CA 1992-2106762	19920416
AT 202708	E	20010715	AT 1992-917374	19920416
IL 101648	A1	19960804	IL 1992-101648	19920419
ZA 9202880	A	19940121	ZA 1992-2880	19920421
US 5385889	A	19950131	US 1993-167052	19931216
US 6770741	B1	20040803	US 1994-359642	19941220
PRIORITY APPLN. INFO.:			US 1991-687959	A 19910419
			US 1992-866246	A 19920414
			WO 1992-US3033	A 19920416
			US 1993-167052	A1 19931216

OTHER SOURCE(S): MARPAT 119:117824

AB Substitution of Pro7 in the peptide hormone bradykinin (H-Arg1-Pro2-Pro3-Gly3-Phe5-Ser6-Pro7-Phe8-Arg9-OH) or analogs with D-hydroxyproline ether or thioether derivs. gives bradykinin antagonists. The preparation of protected hydroxyproline ether and thioether building blocks is also given. These novel bradykinin antagonists show increased enzyme resistance, antagonist potency, or specificity. The prepared analogs are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected such as by insect bites. Thus, O-alkylation of Boc-D-cis-4-hydroxyproline (Boc = Me3CO2C) (preparation given) with allyl bromide, followed by saponification and catalytic hydrogenation gave 45% Boc-D-cis-4-propyloxyproline, which was used in a solid-phase synthesis of H-D-Arg-Arg-Pro-Hyp-Gly-Thi-Ser-D-cis-Hyp(Pr)-Tic-Arg-OH (I; Hyp = L-trans-hydroxyproline; Thi = β -2-thienylalanine; Tic = tetrahydroquinolinecarboxylic acid). I showed $K_i = 172 \pm 45$ nm in a bradykinin binding procedure, and $pA_2 = 5.05$ in a bradykinin antagonist assay.

IC ICM A61K037-42

ICS C07K007-18; C07D207-12

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 2

IT 4530-20-5, N-tert-Butoxycarbonylglycine 13836-37-8 15761-39-4
 18942-49-9, N-tert-Butoxycarbonyl-D-phenylalanine 23680-31-1,
 N-tert-Butoxycarbonyl-O-benzylserine 54631-81-1 56675-37-7
 61315-61-5 147267-14-9 147267-15-0 **147267-16-1** 151602-78-7

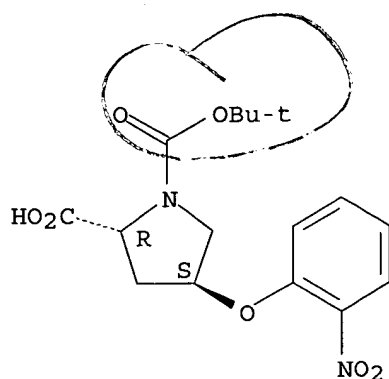
RL: RCT (Reactant); RACT (Reactant or reagent)
 (solid-phase peptide coupling reactions of, in preparation of bradykinin antagonist peptides)

IT **147267-16-1**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (solid-phase peptide coupling reactions of, in preparation of bradykinin antagonist peptides)

RN 147267-16-1 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-nitrophenoxy)-,
 1-(1,1-dimethylethyl) ester, (2R-trans)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 54 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1993:109704 CAPLUS
 DOCUMENT NUMBER: 118:109704
 TITLE: Bradykinin type peptides
 INVENTOR(S): Kyle, Donald James; Hiner, Roger Neal
 PATENT ASSIGNEE(S): Nova Technology L. P., USA
 SOURCE: PCT Int. Appl., 91 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9218155	A1	19921029	WO 1992-US3031	19920416
W: AU, CA, FI, JP, KR, NO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
CA 2106768	AA	19921020	CA 1992-2106768	19920416
CA 2106768	C	20000919		
AU 9219145	A1	19921117	AU 1992-19145	19920416
EP 618809	A1	19941012	EP 1992-911377	19920416
EP 618809	B1	19980819		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
AT 169823	E	19980915	AT 1992-911377	19920416
ES 2123556	T3	19990116	ES 1992-911377	19920416
JP 2002519993	T2	20020702	JP 1992-511395	19920416
JP 3465000	B2	20031110		
IL 101649	A1	19960912	IL 1992-101649	19920419
ZA 9202881	A	19940121	ZA 1992-2881	19920421
US 6288036	B1	20010911	US 1993-167051	19931216
PRIORITY APPLN. INFO.:				
			US 1991-687950	A 19910419
			US 1992-866385	A 19920414
			WO 1992-US3031	A 19920416

AB A pharmaceutical composition for treatment of local pain and inflammation comprises a peptide (bradykinin analog) as a bradykinin receptor antagonist and a carrier. Examples of peptide preparation and a method for evaluation of their bradykinin antagonist activity were given.

IC ICM A61K037-42

ICS C07K007-18

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 34

IT 83623-88-5P 83623-93-2P 83624-01-5P 83624-02-6P 109523-13-9P

146060-16-4P 146060-17-5P 146060-18-6P 146060-19-7P

146060-20-0P 146060-21-1P 146060-22-2P 146060-23-3P

146060-28-8P 146060-29-9P 146060-30-2P 146060-31-3P 146060-32-4P

146060-33-5P 146085-20-3P 146129-07-9P 146955-63-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

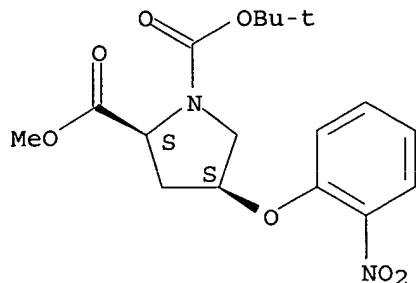
IT 146060-20-0P 146060-22-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 146060-20-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-nitrophenoxy)-,
1-(1,1-dimethylethyl) 2-methyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

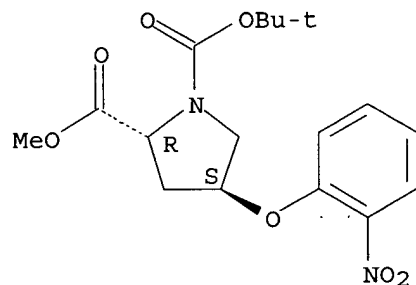
Absolute stereochemistry.



RN 146060-22-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-nitrophenoxy)-,
1-(1,1-dimethylethyl) 2-methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 55 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:222115 CAPLUS

DOCUMENT NUMBER: 108:222115

TITLE: Angiotensin-converting enzyme inhibitors. Mercaptan,
carboxyalkyl dipeptide, and phosphinic acid inhibitors
incorporating 4-substituted prolinesAUTHOR(S): Krapcho, John; Turk, Chester; Cushman, David W.;
Powell, James R.; DeForrest, Jack M.; Spitzmiller,
Ervin R.; Karanewsky, Donald S.; Duggan, Mark;
Rovnyak, George; et al.

CORPORATE SOURCE: Squibb Inst. Med. Res., Princeton, NJ, 08543-4000, USA

SOURCE: Journal of Medicinal Chemistry (1988), 31(6), 1148-60
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 108:222115

AB Analogs of captopril, enalaprilat, and the phosphinic acid

[hydroxy(4-phenylbutyl)phosphinyl]acetyl-L-proline incorporating 4-substituted proline derivs. have been synthesized and evaluated as inhibitors of angiotensin-converting enzyme (ACE) in vitro and in vivo. The 4-substituted prolines, incorporating alkyl, aryl, alkoxy, aryloxy, alkylthio, and arylthio substituents were prepared from derivs. of 4-hydroxy- and 4-ketoproline. In general, analogs of all three classes of inhibitors with hydrophobic substituents on proline were more potent in vitro than the corresponding unsubstituted proline compds. 4-Substituted analogs of captopril showed greater potency and duration of action than the parent compound as inhibitors of the angiotensin I-induced pressor response in normotensive rats. The S-benzoyl derivative of cis-4-(phenylthio)captopril, zofenopril, was one of the most potent compds. of this class and is now being evaluated clin. as an antihypertensive agent. In the phosphinic acid series, the 4-ethylenethioketal and trans-4-cyclohexyl derivs. were the most potent compds. in vitro and in vivo. A prodrug of the latter compound, fosinopril, is also being evaluated in clin. trials.

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 29, 75

IT 75176-37-3P 77282-50-9P 77282-51-0P 81814-64-4P 81814-65-5P
81814-74-6P 81814-88-2P **81872-08-4P** 81872-09-5P
 81872-11-9P 83552-06-1P 83552-23-2P 83552-26-5P 83552-30-1P
 83602-04-4P 83602-05-5P 83623-49-8P 83623-50-1P 83624-12-8P
 83624-20-8P 83624-30-0P 83624-60-6P 83745-60-2P 95399-71-6P
 113564-63-9P 113949-56-7P 113949-57-8P 113949-58-9P 113949-59-0P
 113949-60-3P 113949-61-4P 113949-62-5P 113975-21-6P 114029-53-7P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and angiotensin converting enzyme-inhibiting activity of)

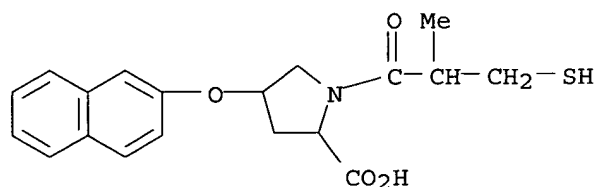
IT 16217-17-7P 75176-19-1P 75776-54-4P 75776-76-0P **81814-75-7P**
 83552-05-0P 83623-48-7P 113949-52-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and saponification of)

IT **81814-74-6P** **81872-08-4P**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and angiotensin converting enzyme-inhibiting activity of)

RN 81814-74-6 CAPLUS

CN L-Proline, 1-(3-mercapto-2-methyl-1-oxopropyl)-4-(2-naphthalenyloxy)-, [1(R*),2 α ,4 α]- (9CI) (CA INDEX NAME)

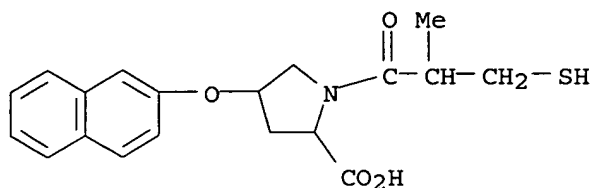


RN 81872-08-4 CAPLUS

CN L-Proline, 1-(3-mercapto-2-methyl-1-oxopropyl)-4-(2-naphthalenyloxy)-, [1(R*),2 α ,4 α]-, compd. with tricyclo[3.3.1.1^{3,7}]decan-1-amine (1:1) (9CI) (CA INDEX NAME)

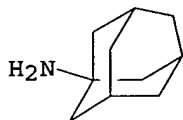
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CRN 81814-74-6
CMF C19 H21 N O4 S

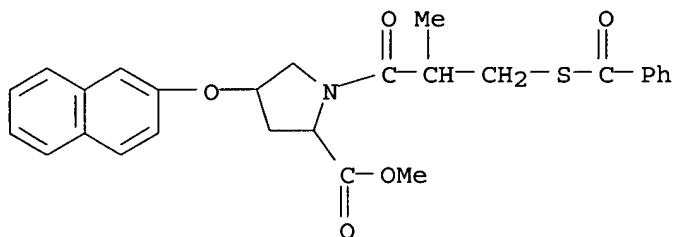


CM 2

CRN 768-94-5
CMF C10 H17 N



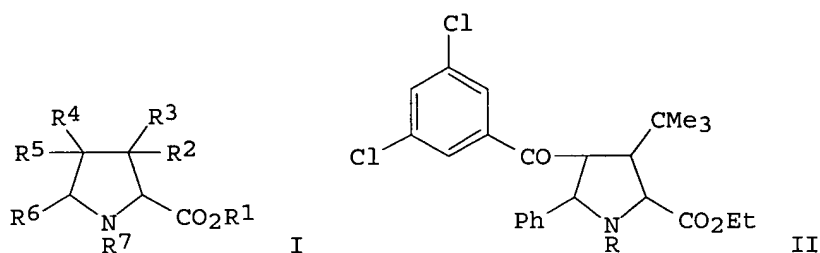
IT **81814-75-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)
RN 81814-75-7 CAPLUS
CN L-Proline, 1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-4-(2-naphthalenyloxy)-, methyl ester, [1(R*),2 α ,4 α]- (9CI) (CA INDEX NAME)



L47 ANSWER 56 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:478822 CAPLUS
DOCUMENT NUMBER: 105:78822
TITLE: Pyrrolidinecarboxylic acid derivatives
INVENTOR(S): Schulz, Guenter
PATENT ASSIGNEE(S): BASF A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 17 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3421295	A1	19851212	DE 1984-3421295	19840608
EP 168607	A1	19860122	EP 1985-106797	19850603
EP 168607	B1	19890208		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
AT 40683	E	19890215	AT 1985-106797	19850603
PRIORITY APPLN. INFO.:			DE 1984-3421295	A 19840608
			EP 1985-106797	A 19850603
OTHER SOURCE(S):		CASREACT 105:78822; MARPAT 105:78822		
GI				



AB The title compds. I [R1, R2, R3 = H, alkyl, haloalkyl, phenylalkyl, halophenylalkyl, R2, R3 = substituted Ph; R5 = alkyl-, haloalkyl-, alkoxy-, or substituted phenylcarbonyl; R6 = substituted Ph; R7 = H, aliphatic, substituted phenylalkyl, phenylcarbonyl, PhCH2O2C], useful as intermediates for pharmaceuticals and plant protective agents, were prepared 2,4-Cl2C6H3COCH:CHCMe3 cyclized with EtO2CCH2N:CHPh in EtOH-EtONa to give II (R = H), acylation of which with MeOCH2COCl in THF containing pyridine and 4-(dimethylamino)pyridine gave II (R = COCH2OMe).

IC ICM C07D207-16

ICS C07D403-04

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 5, 63

IT	103381-95-9P	103381-96-0P	103381-97-1P	103381-98-2P	103381-99-3P
	103382-00-9P	103382-01-0P	103382-02-1P	103382-03-2P	103382-04-3P
	103382-05-4P	103382-06-5P	103382-07-6P	103382-08-7P	103382-09-8P
	103382-10-1P	103382-11-2P	103382-12-3P	103382-13-4P	103382-14-5P
	103382-15-6P	103382-16-7P	103382-17-8P	103382-18-9P	103382-19-0P
	103382-20-3P	103382-21-4P	103382-22-5P	103382-23-6P	103382-24-7P
	103382-25-8P	103382-26-9P	103382-27-0P	103382-28-1P	103382-29-2P
	103382-30-5P	103382-31-6P	103382-32-7P	103382-33-8P	103382-34-9P
	103382-35-0P	103382-36-1P	103382-37-2P	103382-38-3P	103382-39-4P
	103382-40-7P	103382-41-8P	103382-42-9P		
	103382-43-0P	103382-44-1P	103382-45-2P		
	103382-46-3P	103382-47-4P	103382-48-5P		
	103382-49-6P	103382-50-9P	103382-51-0P		
	103382-52-1P	103410-69-1P	103410-70-4P	103430-60-0P	103430-61-1P
	103430-62-2P	103430-63-3P	103430-64-4P	103430-65-5P	103430-66-6P
	103430-67-7P	103430-68-8P	103430-69-9P	103430-70-2P	103452-58-0P
	103452-59-1P	103725-21-9P			

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as pharmaceutical or plant protective agent intermediate)

IT 103382-41-8P 103382-42-9P 103382-43-0P
103382-44-1P 103382-45-2P 103382-46-3P

103382-47-4P 103382-48-5P 103382-49-6P

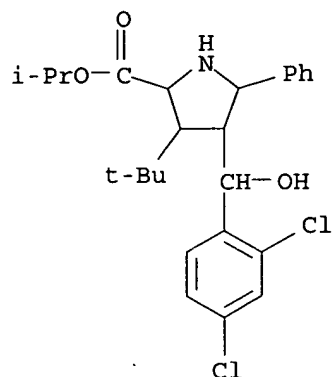
103382-50-9P 103382-51-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as pharmaceutical or plant protective agent intermediate)

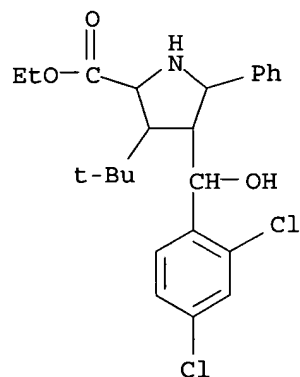
RN 103382-41-8 CAPLUS

CN Proline, 4-[(2,4-dichlorophenyl)hydroxymethyl]-3-(1,1-dimethylethyl)-5-phenyl-, 1-methylethyl ester (9CI) (CA INDEX NAME)



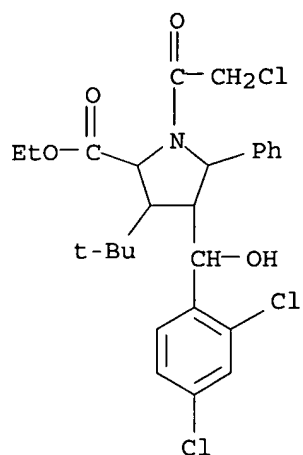
RN 103382-42-9 CAPLUS

CN Proline, 4-[(2,4-dichlorophenyl)hydroxymethyl]-3-(1,1-dimethylethyl)-5-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



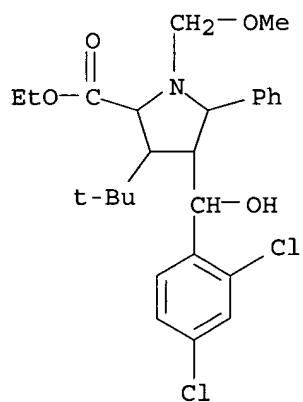
RN 103382-43-0 CAPLUS

CN Proline, 1-(chloroacetyl)-4-[(2,4-dichlorophenyl)hydroxymethyl]-3-(1,1-dimethylethyl)-5-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



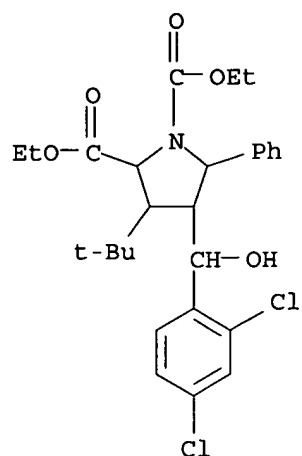
RN 103382-44-1 CAPLUS

CN Proline, 4-[(2,4-dichlorophenyl)hydroxymethyl]-3-(1,1-dimethylethyl)-1-(methoxymethyl)-5-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



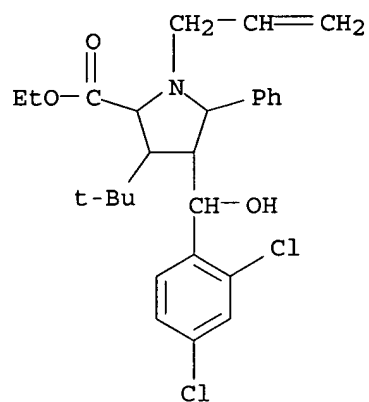
RN 103382-45-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(2,4-dichlorophenyl)hydroxymethyl]-3-(1,1-dimethylethyl)-5-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



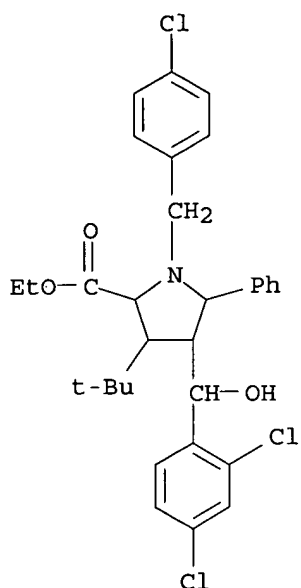
RN 103382-46-3 CAPLUS

CN Proline, 4-[(2,4-dichlorophenyl)hydroxymethyl]-3-(1,1-dimethylethyl)-5-phenyl-1-(2-propenyl)-, ethyl ester (9CI) (CA INDEX NAME)



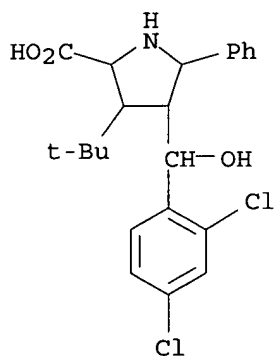
RN 103382-47-4 CAPLUS

CN Proline, 1-[(4-chlorophenyl)methyl]-4-[(2,4-dichlorophenyl)hydroxymethyl]-3-(1,1-dimethylethyl)-5-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 103382-48-5 CAPLUS

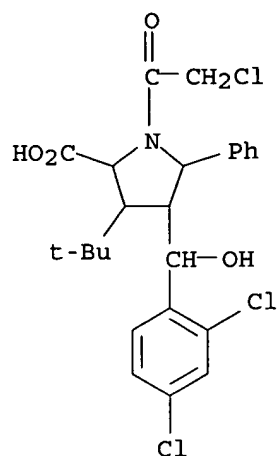
CN Proline, 4-[(2,4-dichlorophenyl)hydroxymethyl]-3-(1,1-dimethylethyl)-5-phenyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

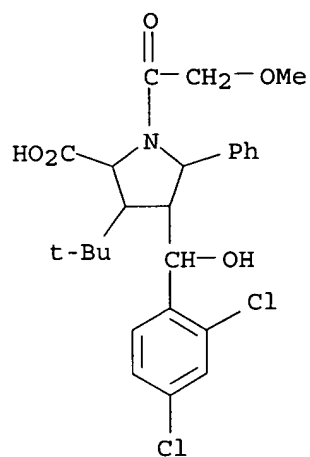
RN 103382-49-6 CAPLUS

CN Proline, 1-(chloroacetyl)-4-[(2,4-dichlorophenyl)hydroxymethyl]-3-(1,1-dimethylethyl)-5-phenyl- (9CI) (CA INDEX NAME)



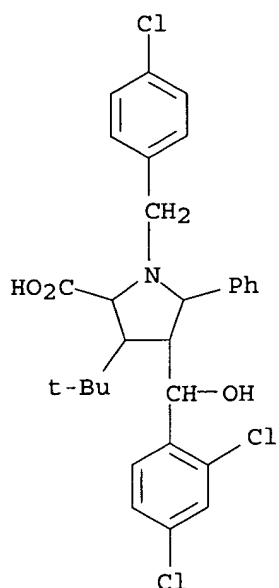
RN 103382-50-9 CAPLUS

CN Proline, 4-[(2,4-dichlorophenyl)hydroxymethyl]-3-(1,1-dimethylethyl)-1-(methoxyacetyl)-5-phenyl- (9CI) (CA INDEX NAME)



RN 103382-51-0 CAPLUS

CN Proline, 1-[(4-chlorophenyl)methyl]-4-[(2,4-dichlorophenyl)hydroxymethyl]-3-(1,1-dimethylethyl)-5-phenyl- (9CI) (CA INDEX NAME)



L47 ANSWER 57 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1985:25039 CAPLUS

DOCUMENT NUMBER: 102:25039

TITLE: Carboxyalkyl amino acid derivatives of various substituted prolines

INVENTOR(S): Petrillo, Edward W., Jr.; Gordon, Eric M.; Krapcho, John; Sprague, Peter W.

PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA

SOURCE: U.S., 32 pp. Cont.-in-part of U.S. Ser. No. 209,563, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

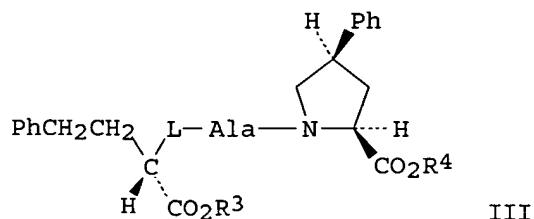
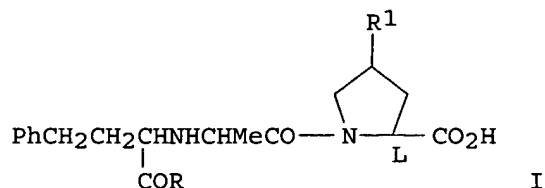
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4462943	A	19840731	US 1981-306553	19810928
CA 1293589	A1	19911224	CA 1981-388933	19811028
ZA 8107601	A	19821027	ZA 1981-7601	19811103
AU 8177087	A1	19820708	AU 1981-77087	19811104
AU 553722	B2	19860724		
EP 52991	A1	19820602	EP 1981-305413	19811116
EP 52991	B1	19870204		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AT 25386	E	19870215	AT 1981-305413	19811116
JP 57116046	A2	19820719	JP 1981-187650	19811120
JP 01058179	B4	19891211		
DK 8105194	A	19820525	DK 1981-5194	19811123
HU 26863	O	19830928	HU 1981-3497	19811123
HU 185986	B	19850428		

PRIORITY APPLN. INFO.:

US 1980-209563	A2	19801124
US 1981-306553	A	19810928
EP 1981-305413	A	19811116

GI



AB Carboxyalkyl dipeptides I (R = OH, OEt; R1 = Ph, SMe, SPh) were prepared as hypotensives (no data) due to their ability to inhibit angiotensin-converting enzyme. Several PhCH2CH2CH(COR)-Ala-X-OH (X = 3-, 4-, 5-, or 4,4-substituted proline residues) were also prepared. Thus, H-L-Ala-OCMe3·HCl was treated with PhCH2CH2COCO2Et in the presence of NaBH3CN in EtOH containing NaOEt to give (S)-PhCH2CH2CH(CO2Et)-L-Ala-OR2 (II, R2 = CMe3), which was de-tert-butylated by CF3CO2H to give II (R2 = H). The latter was coupled with cis-4-phenylthio-L-proline Me ester-HCl by diphenylphosphoryl azide in DMF containing Et3N to give dipeptide III (R3 = Et, R4 = Me), which was saponified to give III (R3 = R4 = H).

IC C07C103-52; A61K037-00; A61K031-40

INCL 260112500R

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 63

IT **81806-12-4P** 82087-67-0P 82087-68-1P 83552-13-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and esterification of, with methanol)

IT 50300-96-4P **81806-11-3P** 82087-66-9P 83551-75-1P

83551-77-3P 83551-82-0P 83552-36-7P 93962-12-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)

IT 83551-76-2P 83551-79-5P 83552-04-9P 83552-07-2P 83552-14-1P

83552-21-0P 83552-24-3P 83552-28-7P **83552-31-2P**

83552-37-8P 83563-25-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with alanine derivative)

IT 83552-05-0P 83552-08-3P 83552-10-7P 83552-15-2P 83552-22-1P

83552-25-4P 83552-29-8P **83552-32-3P** 83552-39-0P

83552-43-6P 83602-03-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)

IT 70984-76-8P 78854-26-9P 83551-84-2P 83551-87-5P 83551-92-2P

83552-02-7P 83552-03-8P 83552-06-1P 83552-09-4P 83552-20-9P

83552-23-2P 83552-26-5P 83552-30-1P **83552-33-4P**

83552-40-3P 83602-02-2P 83602-04-4P 83602-05-5P 83647-97-6P
 93962-38-0P 94061-95-7P 94061-96-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

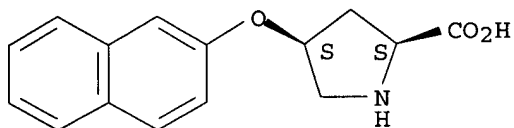
IT **81806-12-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and esterification of, with methanol)

RN 81806-12-4 CAPLUS

CN L-Proline, 4-(2-naphthalenyloxy)-, cis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



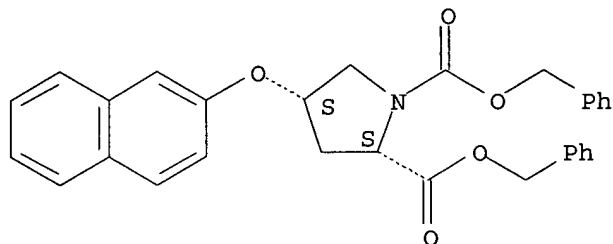
IT **81806-11-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and hydrogenolysis of)

RN 81806-11-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-,
 bis(phenylmethyl) ester, (2S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



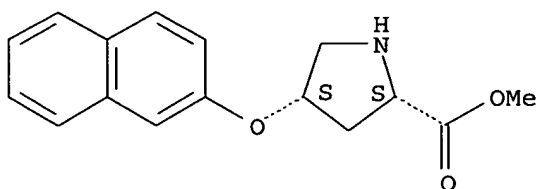
IT **83552-31-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and peptide coupling of, with alanine derivative)

RN 83552-31-2 CAPLUS

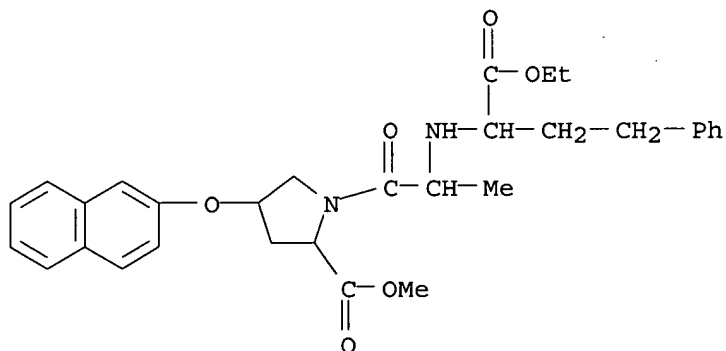
CN L-Proline, 4-(2-naphthalenyloxy)-, methyl ester, hydrochloride, cis- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.

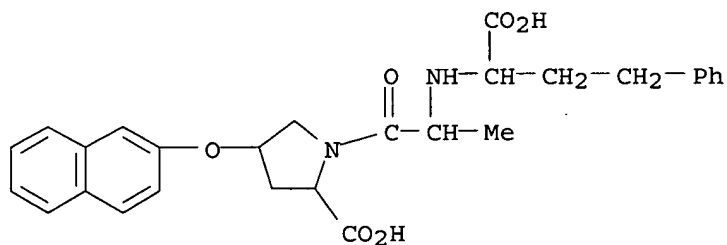


● HCl

IT 83552-32-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT.
 (Reactant or reagent)
 (preparation and saponification of)
 RN 83552-32-3 CAPLUS
 CN L-Proline, 1-[N-[1-(ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-4-(2-naphthalenyloxy)-, methyl ester, [1(R*),2 α ,4 α]- (9CI) (CA INDEX NAME)



IT 83552-33-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 83552-33-4 CAPLUS
 CN L-Proline, 1-[N-(1-carboxy-3-phenylpropyl)-L-alanyl]-4-(2-naphthalenyloxy)-, [1(R*),2 α ,4 α]- (9CI) (CA INDEX NAME)



L47 ANSWER 58 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1984:175285 CAPLUS
 DOCUMENT NUMBER: 100:175285
 TITLE: Substituted 4-phenoxy and 4-phenylthio prolines
 INVENTOR(S): Haugwitz, Rüdiger D.; Sprague, Peter W.
 PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
 SOURCE: Eur. Pat. Appl., 99 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

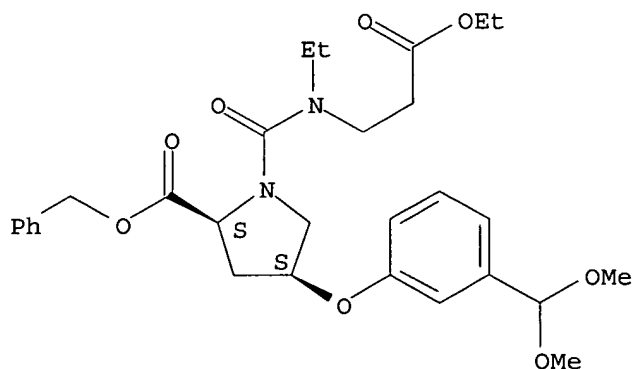
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 95584	A2	19831207	EP 1983-104221	19830429
EP 95584	A3	19840328		
EP 95584	B1	19870107		
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
ZA 8302762	A	19831228	ZA 1983-2762	19830419
CA 1258853	A1	19890829	CA 1983-426141	19830419
AU 8313837	A1	19831103	AU 1983-13837	19830421
US 4681886	A	19870721	US 1983-488491	19830425
JP 58203987	A2	19831128	JP 1983-76078	19830428
JP 04032071	B4	19920528		
PRIORITY APPLN. INFO.:			US 1982-373570	A 19820430
OTHER SOURCE(S):			CASREACT 100:175285; MARPAT 100:175285	
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

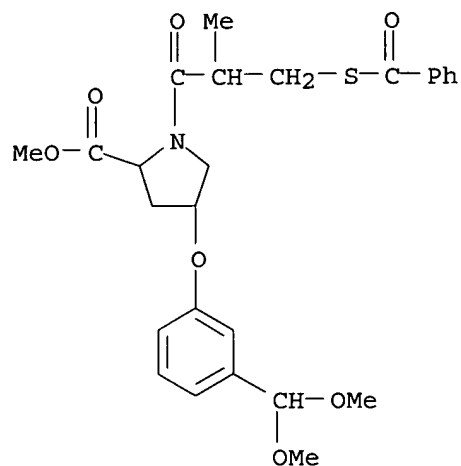
AB Title compds. I [X = O, S; X1, X2 = CHNH, C:N; X3 = CO, SO2; R = H, alkyl, CH2Ph, CHPh2, cation; R1, R2 = H, halo, alkyl, alkoxy, haloalkyl, NO2, SO2NH2; R3 = H, alkyl, cycloalkylalkyl, (un)substituted phenylalkyl, haloalkyl, hydroxyalkyl; R4 = R5SCH2CHR6CO (R5 = H, acyl; R6 = H, alkyl, haloalkyl, Ph, CH2Ph, CH2CH2Ph, cycloalkyl), R8O2CCH2CH2NR7CO (R7 = alkyl, cycloalkyl; R8 = same as R), R9O2CCHR10NHCHR11CO [R9 = same as R; R10 = H, (CH2)mC6H4R12 (R12 = H, alkyl, alkoxy, halo, OH; m = 0-4), (un)substituted alkyl; R11 = H, (CH2)mR12, (un)substituted alkyl], R13P(O)(OR14)CH2CO [R13 = alkyl, (CH2)nR15 [R15 = C6H4R12, thienyl, furyl, pyridyl, cycloalkyl; n = 0-7]; R14 = H, alkyl, CH2Ph, CHPh2, ion, CHR17O2CR16 (R16 = H, alkyl, alkoxy, cycloalkyl, Ph, CH2Ph, CH2CH2Ph; R17 = H, alkyl, cycloalkyl, Ph)] were prepared as antihypertensives (no data) due to their ability to inhibit angiotensin-converting enzyme. Thus, L-4-hydroxyproline was acylated with D-BzSCH2CHMeCOCl to give BzSCH2CHMeCO-Hyp-OH, which was esterified with MeOH/p-MeC6H4SO3H to give the Me ester, which was treated with m-HOC6H4CH(OMe)2 in the presence of Ph3P to give hydroxyproline II. The cyclocondensation of II with benzamide III gave quinazoline IV (R18 = Bz, R19 = Me), which was saponified to give IV (R18 = R19 = H).
 IC C07D403-12; C07D417-12; C07C103-52; C07F009-30; C07D207-16; A61K031-505; A61K031-53
 CC 34-2 (Amino Acids, Peptides, and Proteins)
 Section cross-reference(s): 28, 63
 IT 89813-49-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and cyclization of, with aminobenzamide derivative)
 IT 89813-23-0P 89813-26-3P 89813-29-6P 89813-33-2P

- RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclocondensation of, with aminobenzamide derivative)
- IT 89813-39-8P 89813-43-4P 89813-47-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deblocking of)
- IT 89813-50-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)
- IT 89813-24-1P 89813-27-4P 89813-30-9P 89813-35-4P
89813-37-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)
- IT 89813-25-2P 89813-28-5P 89813-31-0P 89813-34-3P
89813-36-5P 89813-38-7P 89813-40-1P 89813-41-2P
89813-42-3P 89813-44-5P 89813-51-4P
89813-52-5P 89813-53-6P 89813-58-1P 89813-59-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
- IT 89813-49-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, with aminobenzamide derivative)
- RN 89813-49-0 CAPLUS
- CN L-Proline, 4-[3-(dimethoxymethyl)phenoxy]-1-[[3-ethoxy-3-oxopropyl)ethylamino]carbonyl]-, phenylmethyl ester, cis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

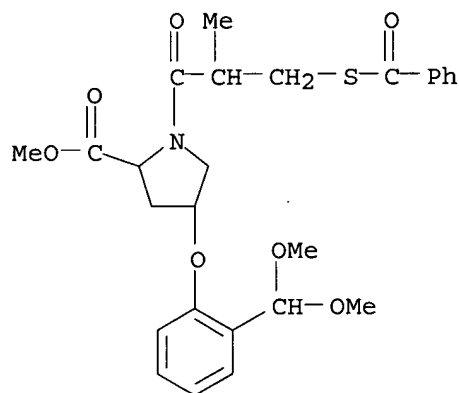


- IT 89813-23-0P 89813-26-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclocondensation of, with aminobenzamide derivative)
- RN 89813-23-0 CAPLUS
- CN L-Proline, 1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-4-[3-(dimethoxymethyl)phenoxy]-, methyl ester, [1(R*),2 α ,4 α]- (9CI)
(CA INDEX NAME)



RN 89813-26-3 CAPLUS

CN L-Proline, 1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-4-[2-(dimethoxymethyl)phenoxy]-, methyl ester, [1(R*),2α,4α]- (9CI)
(CA INDEX NAME)

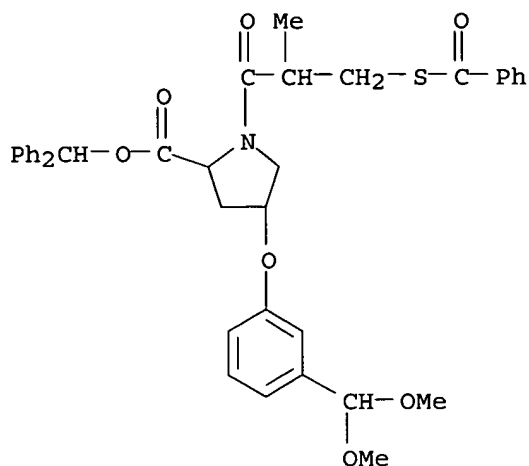


IT 89813-39-8P 89813-43-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and deblocking of)

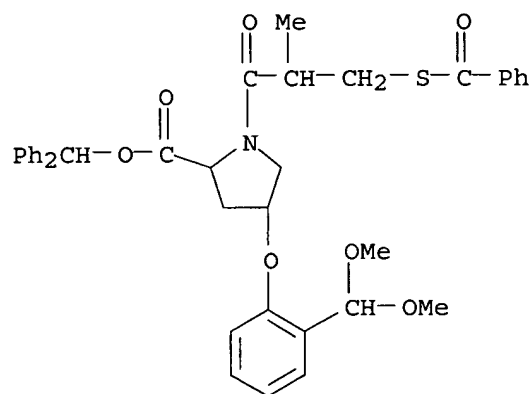
RN 89813-39-8 CAPLUS

CN L-Proline, 1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-4-[3-(dimethoxymethyl)phenoxy]-, diphenylmethyl ester,
[1(R*),2α,4α]- (9CI) (CA INDEX NAME)



RN 89813-43-4 CAPLUS

CN L-Proline, 1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-4-[2-(dimethoxymethyl)phenoxy]-, diphenylmethyl ester, [1(R*),2 α ,4 α]- (9CI) (CA INDEX NAME)

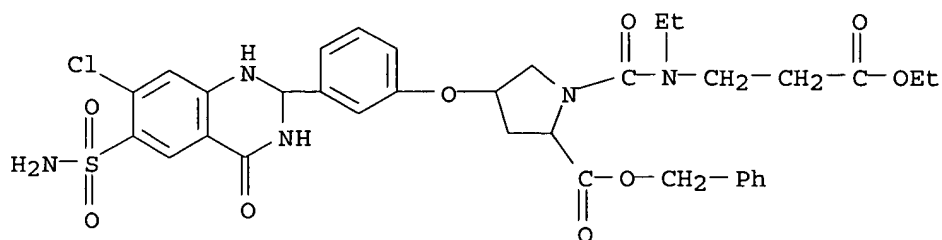


IT 89813-50-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and hydrogenolysis of)

RN 89813-50-3 CAPLUS

CN L-Proline, 4-[3-[6-(aminosulfonyl)-7-chloro-1,2,3,4-tetrahydro-4-oxo-2-quinazolinyl]phenoxy]-1-[[3-(ethoxy-3-oxopropyl)ethylamino]carbonyl]-, phenylmethyl ester, (2 α ,4 α)- (9CI) (CA INDEX NAME)

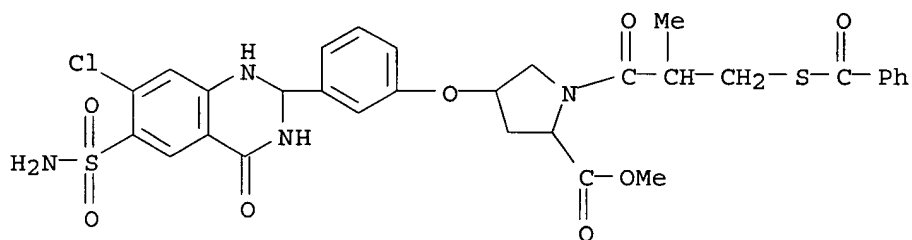


IT 89813-24-1P 89813-27-4P 89813-37-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

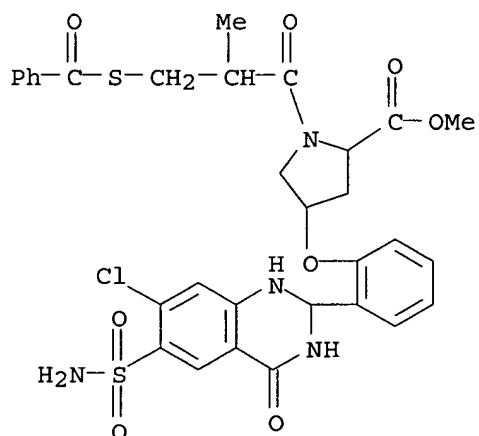
RN 89813-24-1 CAPLUS

CN L-Proline, 4-[3-[6-(aminosulfonyl)-7-chloro-1,2,3,4-tetrahydro-4-oxo-2-quinazolinyl]phenoxy]-1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-, methyl ester, (2 α ,4 α)-(9CI) (CA INDEX NAME)



RN 89813-27-4 CAPLUS

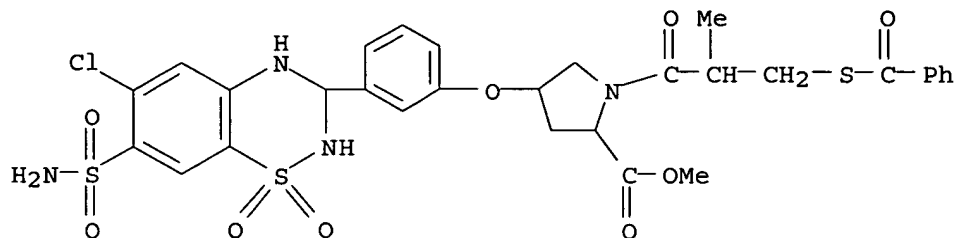
CN L-Proline, 4-[2-[6-(aminosulfonyl)-7-chloro-1,2,3,4-tetrahydro-4-oxo-2-quinazolinyl]phenoxy]-1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-, methyl ester, (2 α ,4 α)-(9CI) (CA INDEX NAME)



RN 89813-37-6 CAPLUS

CN L-Proline, 4-[3-[7-(aminosulfonyl)-6-chloro-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-3-yl]phenoxy]-1-[3-(benzoylthio)-2-methyl-1-

oxopropyl]-, methyl ester, (2 α ,4 α)- (9CI) (CA INDEX NAME)

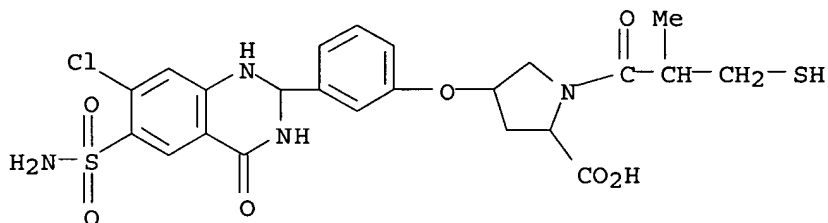


IT 89813-25-2P 89813-28-5P 89813-38-7P
89813-40-1P 89813-42-3P 89813-44-5P
89813-51-4P 89813-53-6P 89813-59-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

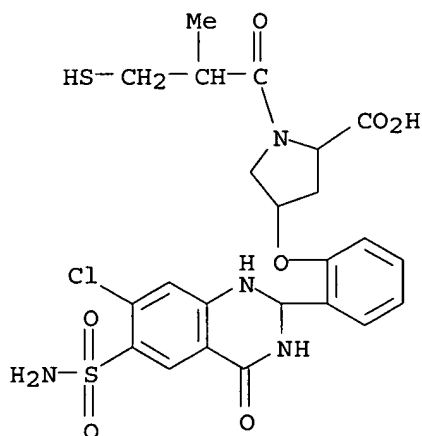
RN 89813-25-2 CAPLUS

CN L-Proline, 4-[3-[6-(aminosulfonyl)-7-chloro-1,2,3,4-tetrahydro-4-oxo-2-quinazolinyl]phenoxy]-1-(3-mercapto-2-methyl-1-oxopropyl)-, (2 α ,4 α)- (9CI) (CA INDEX NAME)



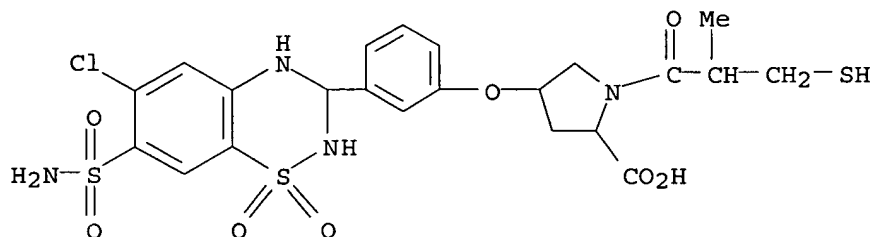
RN 89813-28-5 CAPLUS

CN L-Proline, 4-[2-[6-(aminosulfonyl)-7-chloro-1,2,3,4-tetrahydro-4-oxo-2-quinazolinyl]phenoxy]-1-(3-mercapto-2-methyl-1-oxopropyl)-, (2 α ,4 α)- (9CI) (CA INDEX NAME)



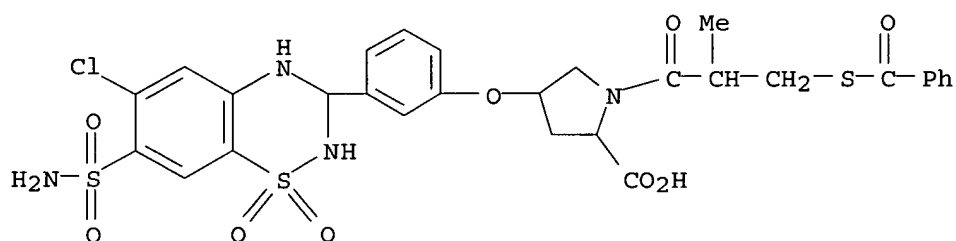
RN 89813-38-7 CAPLUS

CN L-Proline, 4-[3-[7-(aminosulfonyl)-6-chloro-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-3-yl]phenoxy]-1-(3-mercapto-2-methyl-1-oxopropyl)-, (2 α ,4 α)- (9CI) (CA INDEX NAME)



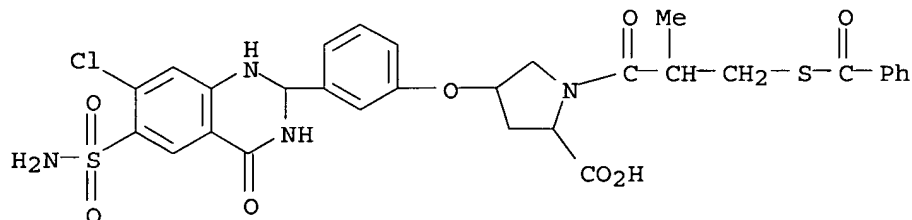
RN 89813-40-1 CAPLUS

CN L-Proline, 4-[3-[7-(aminosulfonyl)-6-chloro-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-3-yl]phenoxy]-1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-, (2 α ,4 α)- (9CI) (CA INDEX NAME)



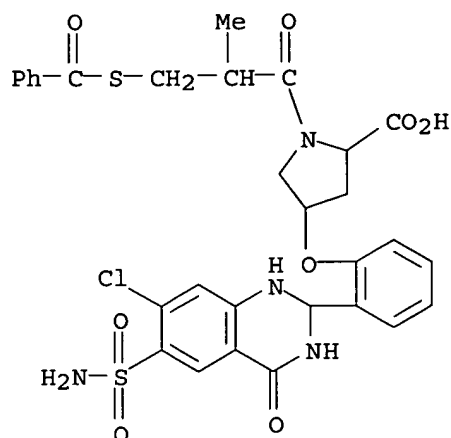
RN 89813-42-3 CAPLUS

CN L-Proline, 4-[3-[6-(aminosulfonyl)-7-chloro-1,2,3,4-tetrahydro-4-oxo-2-quinazolinyl]phenoxy]-1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-, (2 α ,4 α)- (9CI) (CA INDEX NAME)



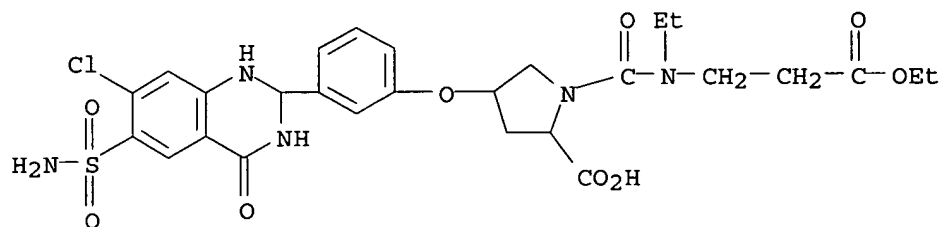
RN 89813-44-5 CAPLUS

CN L-Proline, 4-[2-[6-(aminosulfonyl)-7-chloro-1,2,3,4-tetrahydro-4-oxo-2-quinazolinyl]phenoxy]-1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-, (2 α ,4 α)- (9CI) (CA INDEX NAME)



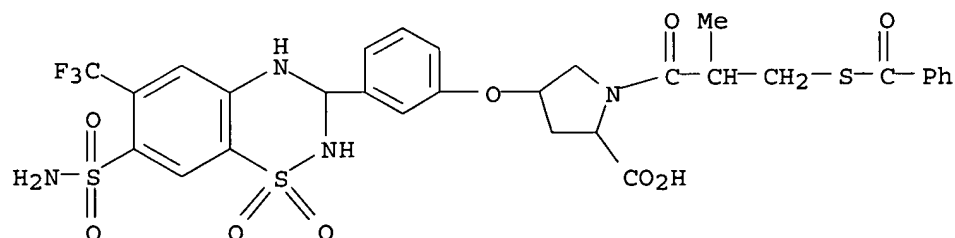
RN 89813-51-4 CAPLUS

CN L-Proline, 4-[3-[6-(aminosulfonyl)-7-chloro-1,2,3,4-tetrahydro-4-oxo-2-quinazolinyl]phenoxy]-1-[[3-ethoxy-3-oxopropyl)ethylamino]carbonyl]-, (2 α ,4 α)- (9CI) (CA INDEX NAME)



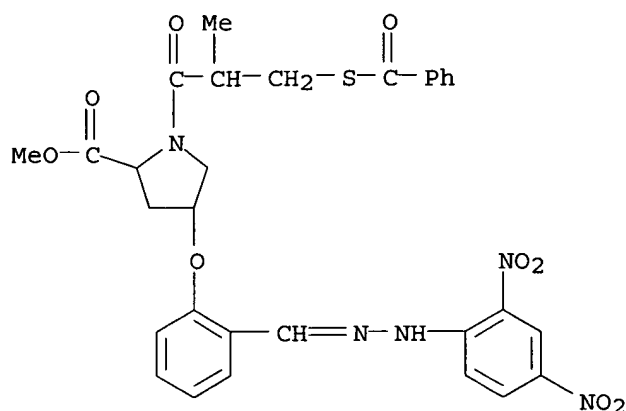
RN 89813-53-6 CAPLUS

CN L-Proline, 4-[3-[7-(aminosulfonyl)-3,4-dihydro-1,1-dioxido-6-(trifluoromethyl)-2H-1,2,4-benzothiadiazin-3-yl]phenoxy]-1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-, (2 α ,4 α)- (9CI) (CA INDEX NAME)



RN 89813-59-2 CAPLUS

CN L-Proline, 1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-4-[2-[[2,4-dinitrophenyl)hydrazono]methyl]phenoxy]-, methyl ester, [1(R*),2 α ,4 α]- (9CI) (CA INDEX NAME)



L47 ANSWER 59 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1983:4790 CAPLUS

DOCUMENT NUMBER: 98:4790

TITLE: Carboxyalkylamino acid derivatives of various substituted prolines

INVENTOR(S): Petrillo, Edward William; Gordon, Eric Michael; Krapcho, John; Sprague, Peter Whitney

PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA

SOURCE: Eur. Pat. Appl., 138 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

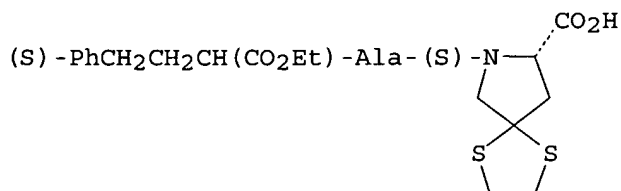
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 52991	A1	19820602	EP 1981-305413	19811116
EP 52991	B1	19870204		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4462943	A	19840731	US 1981-306553	19810928
AT 25386	E	19870215	AT 1981-305413	19811116
PRIORITY APPLN. INFO.:			US 1980-209563	A 19801124
			US 1981-306553	A 19810928
			EP 1981-305413	A 19811116

GI



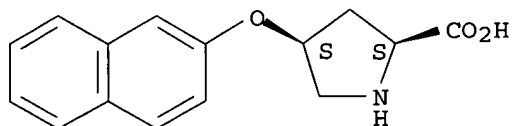
I

AB Antihypertensive (no data) proline derivs. RCOCR₁R₂NHCHR₃COR₄ [R = OH, (un)substituted alkoxy; R₁, R₃ = H, (un)substituted alkyl; R₂ = H, alkyl; R₄ = substituted proline residue] were prepared Thus, the

(ethylenedithio)proline I was prepared from N-benzyloxycarbonyl-4,4-(ethylenedithio)-L-proline, PhCH₂O₂C-Ala-OH and PhCH₂CH₂COCOC₂Et.

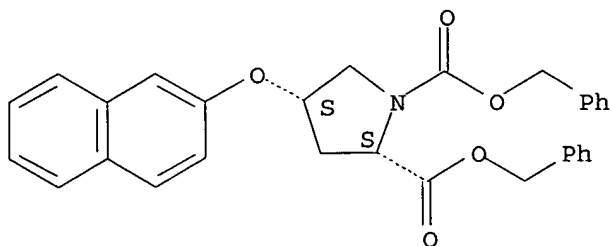
IC C07C103-52; A61K037-02
 CC 34-3 (Amino Acids, Peptides, and Proteins)
 IT 78854-26-9P **81806-12-4P** 82087-67-0P 82087-68-1P
 83552-13-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and esterification of)
 IT **81806-11-3P** 82087-66-9P 83551-82-0P 83551-87-5P
 83552-36-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and hydrogenolysis of)
 IT 83552-07-2P 83552-14-1P 83552-18-5P 83552-21-0P 83552-24-3P
 83552-28-7P **83552-31-2P** 83552-37-8P 83552-42-5P
 83563-25-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction of, with ethoxycarbonylphenylpropylalanine)
 IT 83552-10-7P 83552-15-2P 83552-19-6P 83552-22-1P 83552-25-4P
 83552-29-8P **83552-32-3P** 83552-39-0P 83552-43-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and saponification of)
 IT 83551-80-8P 83551-84-2P 83551-89-7P 83551-91-1P 83551-92-2P
 83551-96-6P 83551-98-8P 83552-00-5P 83552-02-7P 83552-03-8P
 83552-06-1P 83552-09-4P 83552-12-9P 83552-17-4P 83552-20-9P
 83552-23-2P 83552-26-5P 83552-30-1P **83552-33-4P**
 83552-40-3P 83602-02-2P 83602-04-4P 83602-05-5P 83647-97-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 IT **81806-12-4P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and esterification of)
 RN 81806-12-4 CAPLUS
 CN L-Proline, 4-(2-naphthalenyloxy)-, cis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **81806-11-3P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and hydrogenolysis of)
 RN 81806-11-3 CAPLUS
 CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-, bis(phenylmethyl) ester, (2S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



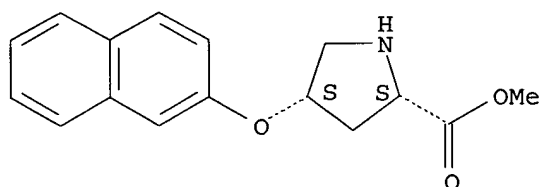
IT 83552-31-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with ethoxycarbonylphenylpropylalanine)

RN 83552-31-2 CAPLUS

CN L-Proline, 4-(2-naphthalenyloxy)-, methyl ester, hydrochloride, cis- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



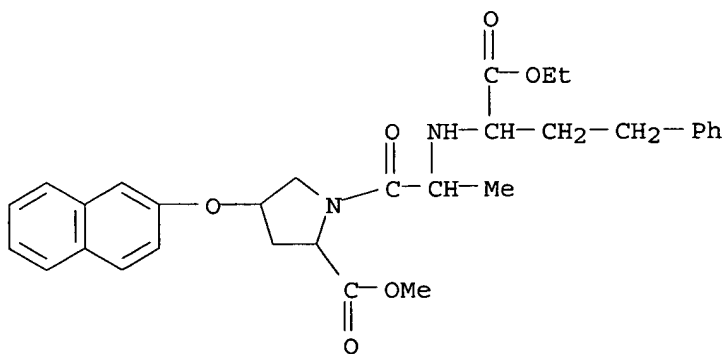
● HCl

IT 83552-32-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)

RN 83552-32-3 CAPLUS

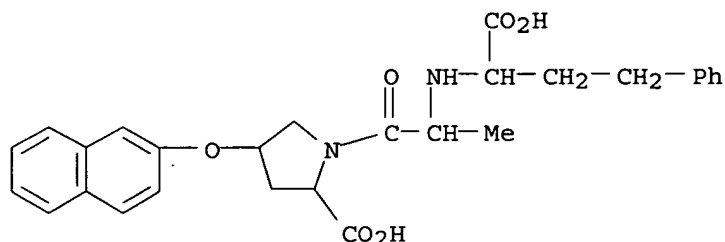
CN L-Proline, 1-[N-[1-(ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-4-(2-naphthalenyloxy)-, methyl ester, [1(R*),2α,4α]- (9CI) (CA INDEX NAME)



IT 83552-33-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 83552-33-4 CAPLUS

CN L-Proline, 1-[N-(1-carboxy-3-phenylpropyl)-L-alanyl]-4-(2-naphthalenyloxy)-
, [1(R*),2 α ,4 α]- (9CI) (CA INDEX NAME)

L47 ANSWER 60 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1982:218225 CAPLUS

DOCUMENT NUMBER: 96:218225

TITLE: Mercaptoacyl derivatives of substituted prolines

INVENTOR(S): Ondetti, Miguel A.; Krapcho, John

PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA

SOURCE: U.S., 31 pp. Cont.-in-part of U.S. Ser. No. 126,239,
abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

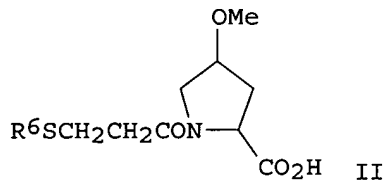
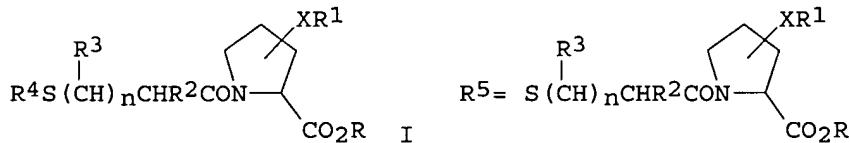
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4316906	A	19820223	US 1980-202801	19801031
PRIORITY APPLN. INFO.:			US 1978-932883	A2 19780811
			US 1979-52691	A2 19790702
			US 1980-126239	A2 19800303

OTHER SOURCE(S): CASREACT 96:218225
GI



AB Title compds. I [R = H, alkyl; R1 = alkyl, alkenyl, alkynyl, cycloalkyl,

1- or 2-adamantyl, (un)substituted Ph, (un)substituted phenylalkyl, (un)substituted 1- or 2-naphthyl; (un)substituted biphenyl; R2 and R3 = H, alkyl, CF3; R4 = H, mercapto group R5; X = O, S; n = 0,1,2] were prepared as antihypertensives (no data) due to their ability to inhibit angiotensin-converting enzyme. Thus, trans-4-hydroxy-L-proline was acetylated with Ac2O to give 98% Ac-Hyp-OH, which was methylated with MeI/AgO to give 66% N-acetyl-trans-4-methoxy-L-proline Me ester, which was hydrolyzed by aqueous Ba(OH)2 to give 50% trans-4-methoxy-L-proline. The latter was acylated with AcSCH2CH2COCl to give 90% proline trans-L-II (R6 = Ac), which was deacetylated by aqueous NH3 to give trans-L-II (R6 = H).

IC A61K031-40; C07D207-12

INCL 424274000

CC 34-2 (Amino Acids, Peptides, and Proteins)

IT 72978-21-3P 75176-22-6P 75176-24-8P 75176-31-7P 75176-35-1P

81806-10-2P **81806-12-4P** 81806-16-8P 81806-53-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and acylation of, with (acetylthio)methylpropionyl chloride)

IT 75176-10-2P 75176-13-5P 75176-15-7P 75176-32-8P 75176-41-9P

81344-67-4P 81814-71-3P **81814-73-5P** 81814-76-8P

81814-81-5P 81846-32-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and deacetylation of)

IT 75176-20-4P 75176-30-6P 81806-09-9P **81806-11-3P**

81806-52-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrogenolysis of)

IT 75176-19-1P 75176-23-7P 75176-34-0P 81806-08-8P 81806-13-5P

81806-49-7P 81814-66-6P **81814-75-7P** 81814-85-9P

81814-89-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and saponification of)

IT 75176-12-4P 75176-14-6P 75176-17-9P 75176-27-1P 75176-33-9P

75176-37-3P 75197-33-0P 75246-75-2P 81806-17-9P 81806-23-7P

81806-24-8P 81806-27-1P 81814-64-4P 81814-65-5P 81814-67-7P

81814-69-9P 81814-72-4P **81814-74-6P** 81814-78-0P

81814-79-1P 81814-80-4P 81814-83-7P 81814-88-2P 81846-33-5P

81846-34-6P 81846-35-7P 81872-07-3P **81872-08-4P**

81872-09-5P 81872-11-9P 81872-21-1P 81938-39-8P 81938-40-1P

81938-41-2P 81938-43-4P 81938-44-5P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)

IT **81806-12-4P**

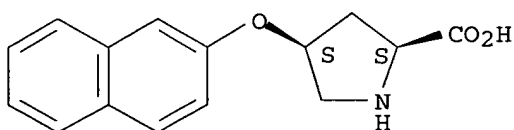
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and acylation of, with (acetylthio)methylpropionyl chloride)

RN 81806-12-4 CAPLUS

CN L-Proline, 4-(2-naphthalenyloxy)-, cis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

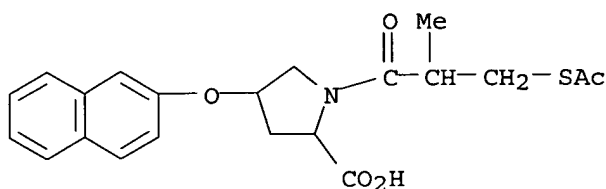


IT 81814-73-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and deacetylation of)

RN 81814-73-5 CAPLUS

CN L-Proline, 1-[3-(acetylthio)-2-methyl-1-oxopropyl]-4-(2-naphthalenyloxy)-,
[1(R*),2 α ,4 α]- (9CI) (CA INDEX NAME)



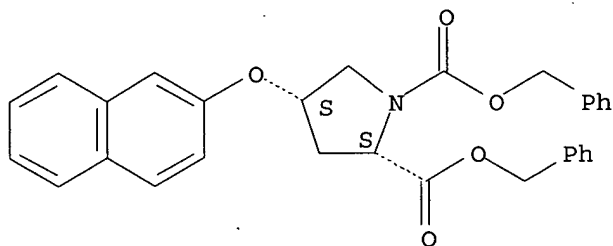
IT 81806-11-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and hydrogenolysis of)

RN 81806-11-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-(2-naphthalenyloxy)-,
bis(phenylmethyl) ester, (2S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

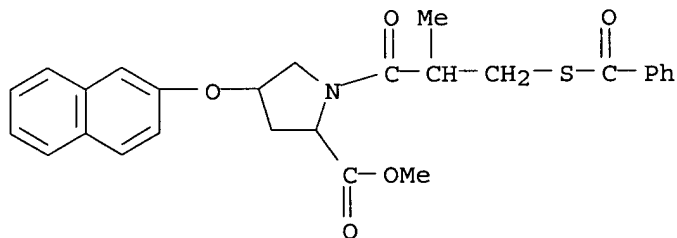


IT 81814-75-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and saponification of)

RN 81814-75-7 CAPLUS

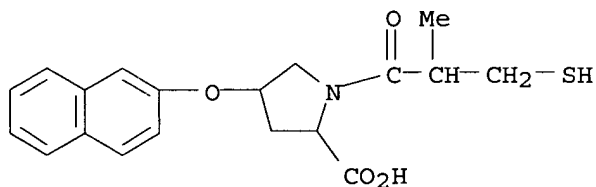
CN L-Proline, 1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-4-(2-naphthalenyloxy)-,
methyl ester, [1(R*),2 α ,4 α]- (9CI) (CA INDEX NAME)



IT 81814-74-6P 81872-08-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 81814-74-6 CAPLUS

CN L-Proline, 1-(3-mercapto-2-methyl-1-oxopropyl)-4-(2-naphthalenyloxy)-,
[1(R*),2 α ,4 α]- (9CI) (CA INDEX NAME)

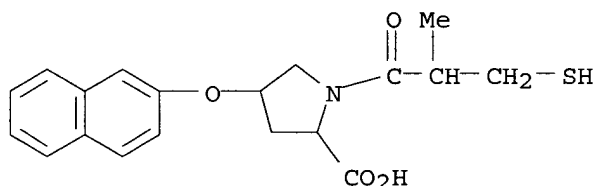
RN 81872-08-4 CAPLUS

CN L-Proline, 1-(3-mercapto-2-methyl-1-oxopropyl)-4-(2-naphthalenyloxy)-,
[1(R*),2 α ,4 α]-, compd. with tricyclo[3.3.1.1^{3,7}]decan-1-amine
(1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 81814-74-6

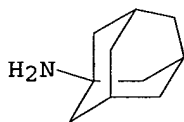
CMF C19 H21 N O4 S



CM 2

CRN 768-94-5

CMF C10 H17 N



L47 ANSWER 61 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1981:581679 CAPLUS

DOCUMENT NUMBER: 95:181679

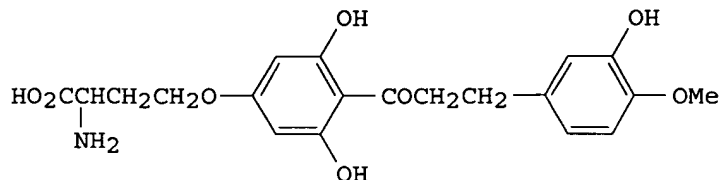
TITLE: Dihydrochalcone sweeteners. Synthesis and sensory
evaluation of a homoserine-dihydrochalcone conjugate
with low aftertaste, sucrose-like organoleptic
properties

AUTHOR(S): DuBois, Grant E.; Crosby, Guy A.; Lee, Janice F.;

Corporate Source:
Source:

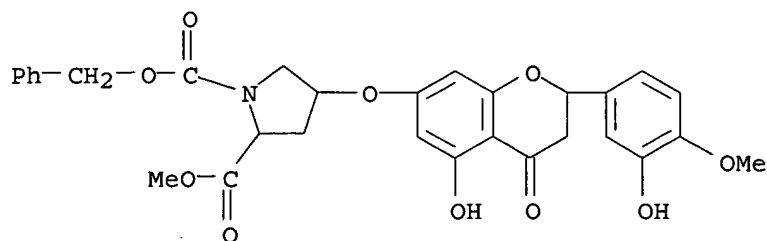
Stephenson, Rebecca A.; Wang, Patricia C.
Chem. Synth. Lab., Dynapol, Palo Alto, CA, 94304, USA
Journal of Agricultural and Food Chemistry (1981),
29(6), 1269-76
CODEN: JAFCAU; ISSN: 0021-8561
Journal
English

Document Type:
Language:
GI



II

- AB Neohesperidin dihydrochalcone (I) [20702-77-6], a potentially sweet compound (340 times the sweetness of sucrose), has a non-sucrose-like, lingering, sweet aftertaste. The analog II [72018-05-4], involving substitution of the neohesperidosyl moiety of I with homoserine ether, was also potentially sweet (400) and the 1st sweet dihydrochalcone to have diminished aftertaste. Three addnl. amino acid-dihydrochalcone conjugates were synthesized and evaluated. Differences in sensory properties were rationalized by changes in hydrophilic-hydrophobic balance as quantitated by the chromatog. parameter k' .
- CC 3-6 (Biochemical Interactions)
Section cross-reference(s): 25
- IT 76338-92-6P 79376-98-0P **79395-62-3P** 79395-63-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)
- IT 72018-05-4P **79376-97-9P** 79377-00-7P 79377-03-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and taste of)
- IT **79395-62-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)
- RN 79395-62-3 CAPLUS
- CN 1,2-Pyrrolidinedicarboxylic acid, 4-[[[3,4-dihydro-5-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-4-oxo-2H-1-benzopyran-7-yl]oxy]-, 2-methyl 1-(phenylmethyl) ester (9CI) (CA INDEX NAME)



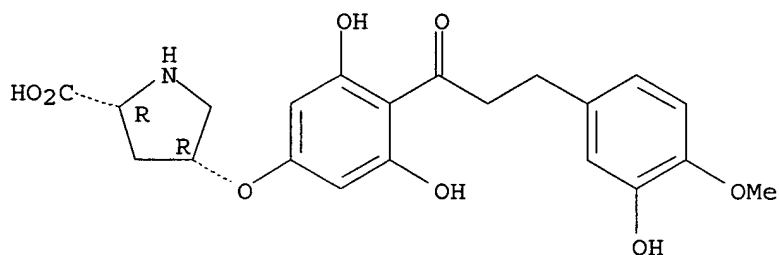
IT 79376-97-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and taste of)

RN 79376-97-9 CAPLUS

CN D-Proline, 4-[3,5-dihydroxy-4-[3-(3-hydroxy-4-methoxyphenyl)-1-oxopropyl]phenoxy]-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

=>